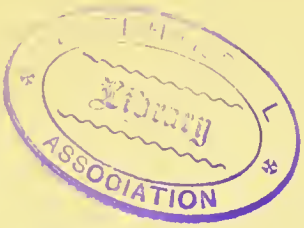
MEDICAL PATHOLOGY OF TUBERCULOSIS

CROOKE



POST GRADUATE LECTURES

ON

THE MEDICAL PATHOLOGY OF TUBERCULOSIS.

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OF

TUBERCULOSIS

(PULMONARY TUBERCULOSIS AND TUBERCULAR PHTHISIS).

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BY

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PATHOLOGY OF TUBERCULOSIS.

LECTURE I.

GENTLEMEN,—The part which I have the honour to undertake in this Post-graduate Course on the Pathology of Tuberculosis has so far been chiefly a practical one, consisting in demonstrations of the methods of staining the tubercle bacillus and of the technique necessary for the histological investigation of tubercle as it comes more or less within the domain of its medical pathology. The remaining part of my task will be to give you as far as I am able, and time permits, a concise description of the varieties of tubercle as we meet with it in the internal organs, but more particularly in the lungs where we shall also have to consider the important question of the relations of tubercle to pulmonary phthisis. I can assure you that I am quite conscious of the difficulties of this task, and I feel that I hardly dare enter upon it without first asking your indulgence for any shortcomings or imperfections that you may detect in my methods of dealing with it. If, for instance, we take the lungs by themselves, the importance of the subject of pulmonary tuberculosis is such, that the literature of it is to be measured by volumes almost innumerable, of which a cursory review alone would more than occupy the time I have at my disposal.

Had I not for reference records of about 150 post

mortems, which I have made in cases of tuberculosis, as well as a large number of preparations illustrating the morbid anatomy and histology of a series of typical examples from them, I should feel that I had but little claim on your attention. And here I desire also to acknowledge my obligations to friends for much invaluable assistance. I am especially indebted to Dr. Sims Woodhead, the director of the research laboratories of the Royal Colleges of Physicians and Surgeons of London, for the loan of a series of beautiful large lung slides; to Messrs. Hall Edwards and J. H. Clayton of this city for microphotographs and drawings made from my own specimens, all of which I hope to be able to demonstrate by means of the lantern. Without help like this I could scarcely have made my lectures sufficiently interesting and instructive.

Thirdly, I feel that my task has already been considerably lightened by the labours of my colleague Professor Barling, who in his first lecture has so ably and so clearly laid before you all the important facts concerning the ætiology and general pathology of tuberculosis, and has, so to speak, thus prepared your minds for a more intelligible grasp of the details connected with its special pathology.

In the special pathology of the disease Professor Barling has dealt chiefly with local tuberculosis of bones, joints, the skin, the external lymph glands, and the genito-urinary system, comprising cases which come under the treatment of the surgeon.

I have to deal with tuberculosis either localised to individual organs, or generalised throughout the system, and to discuss the relationship between these two forms.

We will commence with the lungs, which takes the precedence of all other viscera as a favourite seat of tubercular disease. It is in them that tubercle has been

studied more than in any other organ, and they constitute the battle ground of almost endless debate and discussion concerning the nature and the varieties of tubercular lesions so common in them.

The history of the study of pulmonary tuberculosis may be conveniently divided into two periods, the first of which dates from about the time of Laennec. (1)

It extends over half a century, during which pathologists based their attempts to define the nature of the disease mainly upon anatomical grounds. Then towards the end of the period come the experimental researches of Villemin (2), Burdon Sanderson (3), Wilson Fox (4), and Cohnheim (5), and his pupils, instituted with the object of determining the specific and infective nature of tubercle.

About this time also the relation of micro-organisms to disease was a subject that was absorbing the attention of many scientific pathologists and experimenters.

Its influence in pathological research steadily increased, and became of such importance that it now constitutes a special department of pathology under the title of bacteriology.

It was during the development of this comparatively new science that Robert Koch in 1882 (6) made known his important discovery of a bacillus as the cause of tuberculosis.

With the date of its publication commences the second period in the history of the disease, which is now relegated to a place amongst the class of infective micro-parasitic diseases.

The idea that the virus was to be found in some special micro-organism was not a new one. Klebs and Aufrecht some four or five years before believed they had discovered micrococci as the cause; and Baumgarten, about the time Koch was engaged in completing his investigations, had, as the result of an independent

research also found bacilli that were subsequently proved to be identical with Koch's bacillus tuberculosis. (7)

Nevertheless, it remained for Koch by new and improved technical methods to convert theory into facts, and to establish on a comprehensive basis of expermental evidence the doctrine of the specificity of tuberculosis as it now stands.

Like all new doctrine tending to subvert old ideas it met at first with much scepticism and opposition; but it also raised hopes in the minds of many that time might confirm it (8), and lead to an adjustment of much conflictihg opinion as to the real nature of the disease, if not to a final settlement of a much vexed question on a simple but trustworthy etiological basis. Matters would, indeed, be simplified if we could specify as tubercle all lesions containing the bacillus. Notwithstanding the wide acceptance which Koch's views as to the etiology of the disease have gradually gained for themselves, the real point of issue, viz., how to give a definite answer to the question, "What ought to be called tubercle?" is by no means settled in the minds of pathological anatomists by the relation of the bacillus to the lesions.

Virchow, for example, still defends as tenaciously as ever his definition of tubercle on a purely anatomical and histological basis.

During my recent visit to Berlin I attended frequently the post-mortems held in the Pathological Institute at the Charité, and I found that my conception of tubercle in the lungs from merely a naked eye inspection of it was certainly not always in accordance with the teaching there. I saw around old caseous foci, distributed singly or in groups, the small greyish granulations—some of them showing minute caseous yellow centres—such, indeed, as I had often seen in my own post-mortem

work, and no doubt had described as tubercles. I was told, however, that for the great majority the term tubercle was, strictly speaking, not the correct one to applyto them. They were really and for the most part nodular fibroid thickenings of small bronchi,—fibrous bronchitis and peri-bronchitis,—with small foci of pneumonia around them.

In the light of such teaching it was evident that the use in some of our modern text books (9) of such a nomenclature as "small firm grey miliary tubercle," "large soft grey tubercle," and "yellow tubercle" involved a misapplication of the term.

I began to question how far I could trust my previous histological work as a sufficient criterion to enable me to decide roughly from a naked eye inspection what were tubercles. I was, nevertheless, consoled to learn that even those who were teaching me, with a far greater experience than mine, admitted that it was not possible in all cases to distinguish with certainty by the naked eye alone the tubercles from the non-tubercles. It seemed to me inevitable that every doubtful little nodule in the lungs must pass the closer scrutiny of the microscope before deciding whether it attained the dignity of an anatomically true tubercle.

I must confess that I cannot fully appreciate the utility of such fine anatomical distinctions.

However we may distinguish tubercle, whether on an anatomical basis by the presence of a definite structure, or on an etiological basis by the demonstration of a specific cause in the form of the bacillus, it seems to me that the latter method is the more important from the point of view of practical therapeutics, especially prophylactic treatment. We are now on the verge of future possibilities in dealing with tubercular diseases

to which, in my opinion, no amount of anatomical or histological study alone could have led us.

To the pathological anatomist the word "tubercle" suggests a particular histological picture; the term "tubercular" is a condition qualifying a lesion that at the outset may have nothing to do with tubercle according to his conception of it.

To the pathological mycologist the same terms suggest something more than mere structural details; they imply the presence of the specific cause of the lesion, viz., the bacillus; a conception that has gradually been growing in favour since its discovery.

Now in the lungs we shall find that while the lesions, commonly described as tubercles or tubercular, present differences in their naked eye appearances as well as in their microscopical structure, they are all alike in one respect, *i.e.*, in containing the causal factor of the disease, viz., the bacillus, the demonstration of which is regarded by many modern pathologists (Orth, Ziegler) as the only conclusive proof of what is tubercle.

Let us first of all turn to the pathological anatomist's point of view, and consider briefly the development of the teaching of various schools concerning the rough anatomical characters and minute structure of tubercle in the lung.

At the beginning of the present century Bayle (1810) defined as tubercle in the lungs all nodules, from the size of a hemp seed upwards, that presented an *opaque* greyish or yellowish appearance. He was quite familiar with the disseminated grey miliary form, but on account of the translucency of the nodules hesitated to regard them as tubercle; and in order to distinguish them from tubercles, he gave them the name of "grey granulations."

Laennec, on the other hand, considered them to be the early stage of tubercle, and included them in his

classification. He demonstrated, moreover, the transition of grey into yellow tubercles, and taught that all caseous masses in the lungs, irrespective of size and extent, were really tubercles, whether disseminated or conglomerate and diffuse in distribution.

As the result of investigations into morbid conditions of lung, Addison (10) was really the first to recognise in the larger yellow foci a distinct pneumonic process, to which he gave the name of scrofulous pneumonia.

Tubercle, according to Addison, had its elective seat in the connective tissue septa of the alveoli, or in other words was always *interalveolar*.

A few year later, Virchow confirmed Addison's views as to the existence of a caseous pneumonia, apart from tubercle, and he defined the important part played by this form of pneumonia in pulmonary phthisis.

Tubercle he taught was a non-inflammatory heteroplastic growth, distinctly lymphomatous in type, which originated in the connective tissue. (11)

Virchow's teaching, which is a further development of Addison's, was based upon a more complete histological research, and marks the introduction of the microscope into the systematic study of the disease. The only supposed distinctive feature founded upon microscopical investigation previous to the publication of Virchow's doctrines had been described by Lebert, who believed he had found in the caseous material certain peculiar cellular bodies which he called "tubercle corpuscles." (12)

With improvements in the construction of the microscope, and its more frequent employment in pathological inquiry, we come now to the more elaborate investigations of Buhl (13), Schüppel (14), Wagner (15), Langhaus (16), Hering (17), and Friedländer (18) in Germany, of Thaon (19), Grancher (20), and Cornil (21) in France, of Klein (22), Hamilton (23), and Watson Cheyne (24)

in our own country; and at the same time we must include the opinions of the distinguished clinicians and pathologists who took part in the important debate on the anatomical relations of pulmonary phthisis to tubercle at the Pathological Society of London in 1873. The opinions of all these authorities represent, comparatively speaking, the modern views on the morbid anatomy, and mark a period in the study of the disease, during which the histological investigation of tubercle was worked out with singular care and minuteness of detail at a time when the significance of special structural characters was particularly insisted upon.

I shall have to refer to them pretty frequently.

The Varieties of Tubercle of the Lung.

The purest and most unadulterated example is that form known as *acute disseminated miliary tubercle*, and it is part of a tuberculosis widely diffused throughout the system (acute general tuberculosis).

So far as the lungs themselves are concerned it may be primary or secondary. It is secondary when a general tuberculosis originates from some old caseous lesions existing in the lungs themselves or when it succeeds to a pulmonary tubercular phthisis.

According to the doctrine of the infectiveness of tubercle, its propagation takes place from some primary focus of tubercular disease that may be latent and situated in some part outside the lungs.

Such a focus may be found in the internal lymphatic glands—the mediastinal or retroperitoneal,—or it may be locally manifest as a tubercular disease of bones and joints. The dorsal vertebræ, the ribs or shafts of the long bones, the hip, knee, and ankle joints are common seats of the primary disease.

The tubercular virus finds entrance from the primary focus into the blood stream, either directly into a blood vessel, or indirectly through the lymph paths.

I shall relate a case where a general miliary tuberculosis was set up by the ulceration of a caseous bronchial gland into a branch of the pulmonary artery.

Ponfick has described a case where a caseous mass had ulcerated into the thoracic duct.

In the lungs themselves the dissemination of tubercles may be effected through the walls of the pulmonary vessels. (25) These are instances where the disease is essentially hæmatogenous in its origin.

Of post-mortems that I have made during the last twelve years in a large number of cases of tubercular disease of all forms, I find I have kept for reference records of 147, of which 21 were examples of acute general tuberculosis. Of these 21 cases, I found evidences of pre-existing chronic tubercular lesions outside the lungs in 15, distributed as follows :—

(*a*) Disease of bones and joints 7 cases, spine 3, hip 3, knee 1.

(*b*) Caseous bronchial glands, 4 cases.

(*c*) Caseous retro-peritoneal glands, 2 cases.

(*d*) Caseous foci in spleen, liver, and glands in the portal fissure, 1 case.

(*e*) Tubercular pyelo-nephritis and retro-peritoneal glands, 1 case.

In the remaining six cases, the process started in the lungs either as an acute primary tuberculosis from the outset (in one instance following measles), or it was complicated with tubercular phthisis.

Twelve cases occurred in young children between 3 and 12 years, five in young subjects between 15 and 20 years, and four in adults between 20 and 30 years.

In sixteen, portions of the lungs and other viscera were preserved for systematic histological examination, and accordingly we will now proceed to consider the morbid anatomy and histology of acute disseminated miliary tubercle of the lung.

As a primary disease, *i.e.*, when there are no evidences of any pre-existing lesions, both lungs will be found uniformly affected. They are usually voluminous, retract but little on exposing them, contain abundance of air, and may even be emphysematous, especially along their free borders. The pleura is usually free from signs of inflammation.

On section they are deeply congested, and the cut surfaces are seen to be studded throughout with numbers of small, round, greyish, semi-translucent bodies, about the size of a small pin's head, which are for the most part isolated in distribution, though here and there they may be so closely aggregated as to appear almost confluent. These are the so-called miliary tubercles. Variation in size, form, and general aspect may be noticed in different cases, according to the stage of the disease at which the fatal termination has occurred.

In very acute and rapidly fatal cases, they may be so small and translucent as almost to escape the detection by the naked eye.

When the disease has extended over four or six weeks, they are often larger and more opaque. Many are now distinctly yellow indicating a central caseous necrosis, and they also tend to become more confluent. In consistence they are mostly firm and "shotty" to the feel, and even when so small as to be hardly perceptible, the cut surface of the lung gives a peculiar roughness or granular sensation on passing the finger lightly over it. The reddened intervening pulmonary texture, though containing air, has now lost its normal spongy elasticity and feels more or less resistant and infiltrated. The

condition of the bronchial glands is variable. In some cases they are enlarged and quite cheesy, thus affording undoubted evidence of the priority of the disease in them; in other cases they are merely swollen, vascular, succulent, and infiltrated miliary tubercles evidently contemporaneous to those in the lungs.

Now, what are the microscopical appearances presented by these miliary nodules in the lungs? *Are they in all cases uniform in character, or do they vary?* Before I attempt to answer these questions from the results of the examination of my own specimens, let me divert your attention for a while to the views of some of the more modern authorities on the subject, whose names I have previously referred to.

Schüppel, (26) who was one of the first to undertake a series of elaborate researches concerning the origin and structure of tubercle, formulated a historical description by which it was to be recognised and defined.

His description has been more or less approved by subsequent investigators, and is fundamentally that which is given in most modern text-books on pathological anatomy and histology.

According to Schüppel a true, and fully developed miliary tubercle is made up of certain definite histological elements arranged somewhat as follows :—

(*a*) Centrally are placed large granular and multinucleated giant cells, which are often seen to have branching processes.

(*b*) Immediately around them are disposed other large, roundish or fusiform cells of a similar epitheloid type, provided with a well-defined vesicular nucleus.

(*c*) Arranged in a concentric fashion around the above is a recticulum with oblong meshes, in which are

included numerous small cells, resembling leucocytes or lymphoid corpuscles. The branching process of the giant cells are connected with this peripheral reticulated structure. Lymphoid cells may be seen dotted here and there between the giant cells and epithcloid elements, but it is chiefly at the periphery that they predominate in number within the reticulated meshwork.

Such a concentric arrangement of structural elements has been named by Hamilton (27) "a giant celled system," and is regarded as typical of the "grey miliary tubercle," or the "grey granulation" of Bayle.

Now, a grey miliary tubercle in the lung, the size of a medium sized pin's head, usually corresponds in its entire extent to three or four air vesicles, and may be found to contain as many "giant celled systems" placed in contact with one another by their peripheral zones.

The point which Hamilton insists upon is, that in such a tubercle, the outlines of the alveolar walls are no longer to be made out; they are lost by having become incorporated with the tubercle. He describes the mode of formation of such a tubercle as follows:—

At one point there is a thickening of the alveolar walls produced by the proliferation of its cellular elements, *e.g.*, connective tissue cells and endothelial cells of the capillaries. This increases until it sprouts out into the alveolus, which with it is connected by a pedicle or stalk, then finally it swells out and occupies entire alveolus and becomes organically joined to it. Similar foci of cell proliferation may be seen in various stages of development in the walls of the contiguous alveoli, and they increase until they ultimately coalesce to form the entire tubercle. Giant cells are formed in each

focus by the excessive development of one or two cells at the expense of the others.

Regarding the significance of giant cells, many authorities, particularly Schüppel, Friedländer, and Hamilton have maintained that they are special elements of tubercle.

This view, however, is no longer tenable. They are no doubt very often found in tubercles, but not constantly so; while they have been shown to occur in other formations such as granulation tissue. As to their source, various theories have been advanced. Schüppel (28) who believed that the initial stage of the development of tubercle was the appearance of a giant cell, described them as developing in the interior of blood vessels, but did not give a satisfactory explanation how they derived their nuclei.

Hering looked upon giant cells as representing dilated lymphatics, within which the albumen of the plasma was artificially precipitated in a granular form by the hardening re-agents; the nuclei, which are often disposed in rows at their periphery, he thought were derived from leucocytes or the lining endothelial cells.

Ziegler (29) attributes their formation to the aggregation of leucocytes simply. Arnold, Hamilton, Klein, Watson Cheyne showed that they could originate by the enlargement and the endogenous nuclear proliferation of epithelial cells, the alveolar epithelium. It is certain that there is more than one source for their development.

Concerning the reticular stroma of tubercle, that of the central portion, which is wider meshed, is derived from the intercellular substance, and may be more or less an artificial product resulting from the action of hardening re-agents; that of the periphery, which is

closer meshed and better defined, is derived from the changes in the fibrous connective tissue of the alveolar septa (Buhl).

Now the views promulgated by Schüppel in limiting tubercle to a structure composed of giant celled systems soon met with vigorous opposition from Hering and Buhl.

The former met with cases, running clinically in every respect the course of an acute tuberculosis, and accompanied by the eruption in the lungs of minute nodules exactly resembling miliary tubercles, in which he failed to discover giant cells.

On microscopic examination he found that many of these nodules presented all the appearances of a pneumonia, and as such he regarded them, minute disseminated foci of catarrhal pneumonia. They were cases that ran a very acute and rapid course. Buhl goes so far as to say that every case of acute miliary tubercle of the lungs originates as a desquamative pneumonia, even if the lesions subsequently do undergo a further differentiation into giant cells and a reticulated stroma. And even Hamilton, whose work, like that of his predecessors, was written before the discovery of the bacillus, recognises a pneumonic process. For he describes and figures "a peculiar form of miliary catarrhal pneumonia occurring in children and liable to be mistaken for miliary tubercle."

Klein examined the lungs of seven children dead of acute general tuberculosis. In two of these cases the miliary nodules presented microscopically all the appearances of a pneumonia, in which there was no trace of giant cells anywhere to be found.

In the other five cases he found the reticular giant celled tubercle of Schüppel predominating, and he

regards this as representing later stages of development of the pneumonic variety. He gives beautiful drawings illustrating the microscopical appearances of the lesions.

Klein thinks it is more correct to state that in cases of acute miliary tuberculosis the pulmonary lesions may assume either the form of a miliary pneumonia or the more highly differentiated reticular giant celled structure, according to the stage of development in which it is met with.

I may here say that the results of my own investigations coincide in every way with the admirable description given by Klein of the histology of acute primary miliary tubercle of the lung, and it appears to me that his description holds good even now, for it is corroborated by Ziegler, Orth, and other pathologists in their text-books.

Then again, from a clinical standpoint, I have met with cases of acute general tuberculosis occurring mostly in children in which the lungs are primarily attacked, and the dissemination of the tubercles appears to have taken place along the respiratory channels. These cases last from six to eight weeks, and usually terminate fatally by the development of a tubercular meningitis. The nodular lesions in the lungs are generally much larger than miliary tubercles, often measuring from a tenth to an eighth of an inch in diameter, though, so far as my observation goes, they rarely involve an entire lobule of the lung so as to deserve the name of a caseous lobular pneumonia.

Anatomically they are foci of broncho-pneumonia, larger than the miliary form of pneumonia previously referred to. It is in these cases that I have failed to find evidences of caseating glands or a primary caseous focus, and thus I have been led to

suppose that the infection in the lung was not by way of the blood, but rather by way of the respiratory tract.

I will now relate some cases of primary miliary tuberculosis of the lungs that have come under my own observation; they present the variations in their naked eye appearances and minute anatomical structure which I have just detailed to you.

LECTURE II.

The first case which I have to relate is one of unusual interest, and I will therefore describe it in detail.

A young unmarried woman, about 28, a general servant, was admitted on July 25th, 1889, into the General Hospital, under Sir W. Foster in a moribund condition.

She was more or less comatose, and much too ill to bear anything like a satisfactory physical examination. Dr. T. S. Short, to whom I am indebted for the following account of her symptoms, found her almost pulseless, and suffering from great dyspnœa, her features were dusky and livid ; lips, ears, and finger-tips blue ; the conjunctivæ were yellowish, and her extremities were cold and clammy. Her temperature was nevertheless elevated (102·8), heart sounds almost inaudible, she had moist crepitations all over the chest, back and front, but no marked dulness.

The only history obtainable from those who brought her to the hospital was that she had been ailing for four years, but no details of this illness could be elicited. She began to get worse about three weeks before admission, with increase of dyspnœa, œdema of legs and face, swelling of the abdomen, jaundice and blueness of lips. During the last week she had got rapidly worse. She died two hours after her admission.

Post-mortem examination revealed a well-marked

stenosis of the mitral valve, the orifice admitting only the tip of the little finger.

There was a small patch of ulceration on the auricular surface of the posterior segment of the valve ; the aortic valves were thickened and fringed with a few small recent vegetations (acute verrucose endocarditis). *Both lungs* were deeply congested, rather tough and leathery in consistence, and presented in all respects the characters of a mechanically congested lung of long standing (brown induration).

On section they were seen to be studded all over with *very minute translucent granules*, looking at first glance like very small droplets of water or bubbles of air, or the minutest frog spawn.

In fact, it was by mere accident that they were recognised by allowing the light to fall somewhat obliquely on the cut surface, and in any hurried examination they might easily have been missed. At first, on account of their minuteness and unusual appearance, I was in doubt as to what they really were, and in such a condition of the lungs, the result of a stenosed mitral valve, I never thought of miliary tuberculosis. Finding them, however, in both lungs on the surface of every section through them, I at once made some sections with the freezing microtome, stained them in picrocarmine, and mounted them in iodised serum. On examination with the microscope, there was no doubt that each of these minute translucent points corresponded with a small focus of pneumonia. On further staining sections with carbol-fuchsine according to Ziehl-Neelsen's method, I found that each pneumonic focus contained tubercle bacilli, and these at once cleared up all doubts as to the nature of the miliary lesions. On searching for some primary focus of infection, I found the bronchial glands on both sides swollen, pigmented, and caseous on section, and on the left side one of these was firmly attached to

a branch of the pulmonary artery through the wall of which it had ulcerated. Tubercle bacilli were also found in sections of the caseous bronchial glands.

On examining the brain the meninges were very hyperæmic; there was no actual exudation of inflammatory lymph, though here and there very minute greyish semi-translucent granules were seen scattered in the pia-arachnoid along the course of the vessels. On microscopic examination they were found to be very early miliary tubercles, consisting for the most part of fusiform dilatations and cell infiltration of the lymphatic sheaths of the blood-vessels.

Some were beginning to necrose, and in all examined tubercle bacilli were demonstrable.

Liver and spleen were enlarged, the former presenting markedly the appearances characteristic of cyanotic and nutmeg liver, the latter merely swollen and engorged, but in neither were tubercles visible *with the naked eye.*

The kidneys were slightly enlarged, both together weighing 11½ ozs.:—They were firm in consistence, the capsules were a little sticky in places, surfaces of a fawn colour and spotted with punctiform extravasations; here and there they presented opaque greyish dots of infiltration, about the size of a pin's head, or even larger, each of which was encircled by a zone of hyperæmia. Although none of them were found softened or breaking down, they looked more like foci of infiltration, the result of capillary embolism, than tubercles, and the microscope confirmed this, for each spot was a minute focus of interstitial inflammatory cell infiltration containing both micrococci and bacilli, the latter larger than, and not staining like, the tubercle bacillus. Their causation could only be referred to the small patch of ulcerative endocarditis found on the posterior segment of the mitral valve.

Let us now once more turn to the lungs, portions of

which were hardened in Muller's fluid and alcohol for a subsequent and more complete histological examination.

Sections were made both with the Swift-William's freezing microtome, and also, after imbedding in celloidin, with the Schanze microtome. Some were doubly stained with picrocarmine and hæmatoxylin; others were stained with carbol-fuchsine for tubercle bacilli and counterstained with methylene blue. Under the microscope the miliary lesions, though present in immense numbers are mostly discrete in distribution, they are characterised by their small dimensions. On measurement very few exceed the twenty-fifth of an inch in diameter (a millimetre), while the smallest are barely 1/100 inch. On the average they measure 0·02 to 0·03 inch (metric system 0·15 to 0·45 millimetre); each consists simply of a mass of proliferated cells, in the centre of which necrosis is in progress, and the outlines of the alveolar walls are indistinguishable. The necrotic part is composed of a homogeneous or faintly fibrillated granular substance, in which are imbedded nuclei of all shapes and sizes, together with a few disintegrating red blood cells. At the periphery, the alveolar walls become quite distinct, the individual cell forms of the intra-alveolar exudation are well defined, and consist mainly of (*a*) swollen and proliferating alveolar epithelium with large round or ovoid nuclei, staining well with hæmatoxylin; (*b*) exuded leucocytes with their characteristic deeply stained nucleoli; and (*c*) extravasated red blood cells also mixed up with the proliferating epithelium. In some alveoli fibrin is present. The larger foci cover from four to six alveoli, the smaller are limited to even one or at most to three. In these latter, the proliferation of the alveolar wall and its extension to the alveolar epithelium, the individual cells of which are collected into half or quarter moon shaped masses, is quite conspicuous. In the interverning pulmonary parenchyma, cellular infiltra-

tion and thickenings of the alveolar walls are marked features. *Now in none of these miliary lesions are giant cells to be found*, and at the same time in none of them (*i.e.*, in sections stained with fuschine and methylene blue) are tubercle bacilli absent. In the larger foci where caseous necrosis is evident they are present in large numbers.

Besides the tubercle bacilli, other shorter and thicker bacilli, staining well with hæmatoxylin or methylene blue, are found mostly within blood vessels and immediately outside them. It is also noticeable that the tissue in their immediate vicinity looks necrotic or partially dead, for it stains very faintly.

What the significance of these bacilli may be, I cannot say definitely. Very probably they possess no pathogenic importance whatever, but are simply putrefactive or saprophytic organisms.

It should not be forgotten that the post-mortem examination was made within eighteen hours after death in warm weather. They resemble very closely the bacillus saprogenes No. 1 of Rosenbach (30) in possessing rounded ends. At all events they contrast conspicuously with the slender aud ruby red stained tubercle bacilli.

Regarding the situation of the milary lesions; (1) they are frequently disposed around small blood vessels, which, in some instances, are seen thrombosed and occupying the centre of the nodule; (2) they are also seen in the adventitia of the larger arteries and growing from the interlobular septa; (3) lastly they may be found sprouting from the walls of the alveoli.

The points then of special interest in this case are :—

First.—Its unusually complex character, viz., a combination of mitral stenosis, miliary tuberculosis and ulcerative endocarditis. Tubercular lesions occurring in heart disease are rare events, in fact, it is generally laid down that heart disease, particularly mitral stenosis,

induces a condition of the lung that is quite unfavourable for the development of tubercular or phthisical processes.

I can call to mind only two other cases where mitral stenosis was associated with pulmonary tubercular phthisis and cavity formation, though in neither was the stenosis so marked as in this one.

Secondly.—The latent character of the tubercular disease in the caseous bronchial glands is another noteworthy feature.

It is possible that this patient at some period in her life was the subject of tubercular disease, which had cleared up in the lungs, but was arrested in the bronchial glands, where it was latent and smouldering, to become reignited when her general powers of resistance had run down from the effects of hard work, combined with other morbid conditions. Unfortunately no information could be obtained to explain the mitral stenosis, whether it was rheumatic or congenital in its origin. At all events had this patient come before us a year or so previously, we should in all probability have diagnosed her cardiac affection, but who would have ventured an opinion as to the existence of tubercular disease other than a negative one. The case, I think, has an important bearing upon the new method of treating tubercular disease by the injection of tuberculin, especially so in reference to cases that neither outwardly nor inwardly, according to all our methods of physical diagnosis, show evidence of tubercular disease and yet exhibit a general febrile reaction after injections of the lymph. It likewise suggests a search through post-mortem records for similar cases of latent tubercular disease, for any information that could be thus collected would be of value in reference to Koch's method of treatment.

Lastly, the histological characters of the miliary lesions deserve special mention. From a clinical and

practical point of view we had here an undoubted case of acute miliary tubercle of the lung, distinctly hæmatogenous in origin, and yet the lesions presented no trace whatever of giant cells and a reticulated structure, on which some authorities insist as essential for the pathological diagnosis of tubercle. It affords strong support to the views of Buhl, Hering and Klein, and demonstrates, at all events, that acute miliary tubercle of the lung in one of its manifestations may assume the form of a pneumonia. In fact the designation acute miliary tubercular pneumonia seems to be a more appropriate one to this case. It is quite possible, however, as Klein suggests, that, had the case not run so acute a course we might have met with examples of the reticular giant celled structure. I must regret that I unfortunately omitted to examine the endocarditic lesions of the valves for micro-organisms and for the tubercle bacillus, so as to have made the case more complete.

The next case, though undoubtedly acute in character was of longer duration, and the tubercles had undergone modifications of structure which I shall describe after giving you an epitome of the history and symptoms. Old caseous foci existed also here in the bronchial glands and in the spleen. Two clinical facts worthy of notice are: (1.) The marked symptoms and signs of pulmonary mischief. (2.) And the subsequent manifestation of symptoms of meningitis shortly before death.

A. W., a boy, nine years of age, with no history of consumption in the family, all the members living and healthy, had been at home eight weeks suffering with pains in both sides of the chest, cough, night sweats and rapid emaciation; except small-pox five years ago he had no previous illness. On admission there was a marked hectic flush on the cheeks, temp., 103; pulse, 132; resp., 36. Large moist râles were heard all over the chest on both sides; at the left apex and on the right side behind

over the scapular region the percussion resonance was deficient, vocal resonance increased, breath sounds were harsh, and expiration prolonged. During the first week the pain in the chest, cough and night sweats continued without abatement, the temperature curve was very irregular, varying from 99° and 101° in the morning to 103° and 104° in the evening. On the sixth day he had a convulsive seizure accompanied by a fall in the temperature and twitchings of the right arm. The last two nights he became unconscious and delirious, screaming out loudly at intervals. Bowels constipated throughout. Death occurred in the tenth week from the commencement of the illness. Necropsy: Miliary tubercles scattered in the pia-arachnoid along the course of the vessels, but unaccompanied with any exudation of much inflammatory lymph.

Lungs weighed together 36 ozs. Both stuffed throughout with soft grey tubercles. The disease is much more advanced in the superior lobes where the tubercles are closely set, coalescent, opaque, yellow and caseating, and the intervening pulmonary texture seems to be the seat of much recent catarrhal pneumonia. Such portions sink in water. In the lower lobes the tubercular infiltration is more discrete, and the tubercles are greyish, translucent, and show no signs of caseation. Such portions float in water. Bronchial glands enlarged and caseous. Spleen four ounces. Two old caseous nodules imbedded in its substance. The rest of the organ everywhere infiltrated with closely set grey translucent tubercles. The appearances on section somewhat resembled those of sago grains imbedded in the substance (sago or amyloid spleen on a smaller pattern). Numerous miliary tubercles in the liver and kidneys, and a few early ones in the mucous membrane of lower part of ileum, but no ulceration.

Regarding the microscopic appearances of the tubercles in the lungs :—

They are uniformly rounded or ovoid in shape and well defined; all are considerably larger than those in the previous case, measuring never less than 0·03 inch, and on the average 0·05 to 0·07 inch in diameter. All the larger ones present an extensive caseous centre, which, in some instances, has fallen out in the preparation of the specimen, thus leaving a microscopic cavity. This caseous centre is composed of an amorphous granular débris, together with disintegrating nuclei stained deeply with hæmatoxylin, it is in all cases limited by a zone of proliferating connective tissue, rich in cells and nuclei; the latter being for the most part large, oval or fusiform, and vesicular.

In none of the tubercles can any trace of the alveolar structure of the lung be distinguished.

In this, as in the first place, the tubercular process is acute in character and probably the result of bacillary emboli in small blood vessels and capillaries. It has commenced in the walls of the infundibula or bronchioles as an inflammatory proliferative process, extending peripherally. The interior of the infundibula (or alveolar ducts) and of the bronchioles has become blocked by a cellular exudation that has undergone a rapid necrosis, and thus in the larger tubercles the central caseous necrotic mass corresponds to the lumen of such an infundibulum, while the peripheral zone represents the wall greatly thickened and altered by the cell proliferation. Many of the oval or spindle-shaped nuclei are the offspring of the nuclei of the connective tissue and muscle cells normally found in the walls of the bronchioles and infundibula.

The walls of the intervening pulmonary alveoli are much thickened by small celled infiltration and the interior filled by large proliferating epithelial cells (alveolar epithelium). Tubercle bacilli are seen in great

profusion both in the tubercles and also in the contiguous alveoli amongst the cells.

Indications of giant cells or imperfectly developed forms of them are found *only in the smaller non-caseating tubercles*, in the larger ones they are entirely absent.

In some instances the tubercles are seen distinctly growing in the adventitia of a small blood vessel, or at the borders of the interlobular septa.

This case presents to us a more advanced stage in the development of the process than in the first one.

The remaining affected viscera were examined microcopically for tubercles and tubercle bacilli with confirmatory results.

The next group is, so far as my own experience goes, a small one, of which I will show you specimens from two typical examples. Both lungs were uniformly affected. Here the miliary tubercles, which are primary, conform as regards their minute anatomy to the classical descriptions of Schüppel, Hamilton, and others, in presenting the giant celled reticular structure.

They were found to be small, firm, greyish, semitranslucent nodules, exhibiting to the naked eye but little tendency to caseation, and disseminated both in an isolated form as well as in small racemose groups consisting of from three to five individual tubercles that had become confluent. The pulmonary texture appeared to be little if at all altered by other associated morbid changes. Microscopically the tubercles measure from 0·02 to 0·03 inch, seldom exceeding the latter in diameter. Each is made up of several "giant-celled systems" grouped around a *small* caseous centre. The peripheral adenoid reticulum or sheath surrounding each entire nodule is well defined.

From an examination of sections I have recently made of the lungs of these cases, pieces of which I found among my collection of material preserved for histological pur-

poses, tubercle bacilli are demonstrable in some, but not all the tubercles, and are not anything like so profuse in distribution as in the first two cases described.

The bronchial glands were enlarged, caseous, but also infiltrated with the miliary lesion.

Clinically, these cases were examples of primary chronic tuberculosis of the peritoneum and abdominal lymph glands—tabes mesenterica—with tubercular ulceration of the intestine, and a general tuberculosis, *more of a subacute type* had developed and become engrafted upon the primary affection, for recent miliary tubercles were found in the peritoneal coat of the intestines.

Tubercular meningitis occurred in both, and in one a small caseous mass was found in the substance of the left temporo-sphenoidal lobe of the brain. The tubercular eruption in the meninges was accompanied with an abundant exudation of inflammatory lymph, so that the help of the microscope was necessary in order to detect the tubercles.

So far as concerns the history of these cases, I have only a few notes by me, both occurred in children under ten years of age, and they came under my observation some years ago at the Leeds Workhouse Infirmary, where they were under treatment for three or four months. The symptoms were at first those of the local affection, viz.:—

Swelling, pain and tenderness of the abdomen, pyrexia of a sub-febrile and irregular hectic type, night sweats, profuse diarrhœa and emaciation. The termination was somewhat abrupt with the development of the meningitis, *but the pulmonary physical signs throughout were mostly of a negative character.*

In these cases the origin of the tubercles in the lungs may have been partly hæmatogenous and embolic, but the differentiation of their structure was the result of

slower growth and development, and thus it is possible that some of them spread by way of the lymphatics.

The last group of the series of cases of acute pulmonary miliary tuberculosis includes a small number where the organs, first attacked by tubercular disease, were the lungs themselves. They thus differ from the others etiologically in the fact that the disease was not, so far as could be determined, traceable to some pre-existing focus in another part of the body, whence it spread by way of the vascular or lymphatic channels to the lungs, but the tuberculisation of the system generally was secondary to the pulmonary affection.

Clinically, the cases presents to us an acute form of pulmonary, developing into a general tuberculosis, and running a fairly rapid course from the commencement. The subjects of the disease were mostly children from five to ten years of age, admitted quite in the early stage of the illness, and under observation from seven to eight weeks. In three cases no history of phthisis in the family or of previous illness in the patient was obtainable, but one of them came from a house where the mother was reported to have died from typhoid fever five weeks before.

The child had been ill at home for nine days with diarrhœa, and for the first fortnight after admission into the Hospital his illness simulated typhoid, diarrhœa remaining a prominent symptom throughout.

In the fourth case the patient had only just recovered from an attack of measles, and there was a family history of phthisis. In all, the local signs and symptoms of the pulmonary mischief were evident from the first, viz. :—

Troublesome cough without expectoration, pain in the chest, rapid breathing, inequality and impairment of the percussion resonance accompanied with moist crepitations and exaggerated expiration almost bronchial in character.

In two, a temporary abatement of the local and general symptoms was observed, followed, however, by a marked exacerbation and the development about the fifth or sixth week of meningitis, that was the cause of the fatal termination in all the cases.

Post-mortem, the lungs were found stuffed with soft grey tubercles all of which—even the isolated ones—were specially noted as being larger than the usual grey miliary variety. The post-mortem report in two cases says:—"But the individual tubercles are of a rather large size, much more so than millet seeds, or the size of disseminated grey granulations usually seen. Many are as large as a No. 3 shot corn."

The disease was more advanced in the superior and the upper part of the inferior lobes, where the tubercular infiltration was more confluent, and the tubercles were becoming yellow caseous, and even breaking down in the centre into small cavities filled with a greenish yellow pus containing tubercle bacilli in considerable numbers.

Miliary tubercles were found in the meninges, in liver, spleen and kidneys. The condition of the intestine varied, in one case (an adult) there was distinct ulceration, in the child with diarrhœa just mentioned, there was no ulceration but swelling of Peyer's patches and the solitary follicles. In the other cases the intestines had escaped.

In none were the bronchial or abdominal lymphatic glands caseous. They were enlarged and infiltrated with tubercles not older in appearance than those elsewhere.

In fact no distinct caseous focus was anywhere discoverable in these cases.

Histological examination of the lungs showed that the tubercles in all were nodules of tubercular or caseous bronchitis and peri-bronchitis, such as we shall find to be

the predominating lesion in, and describe more fully when considering tubercular phthisis.

Many of the larger nodules (even in the lung of a young child of five years) measured from 1-10th to 1-8th of an inch in diameter. The smaller ones involving the bronchioles or alveolar passages were about half the size.

Giant cells were found only in the cellular thickening around the extensive caseous centres.

This concludes the description of the pulmonary lesions in the series of cases *that, from a clinical standpoint were all of them examples of acute general tuberculosis.*

I have, I think, brought forward sufficient evidence even in my own cases, limited as they are in number to show, that the lesions conform to no one particular type of structure, but undoubtedly present differences in their naked eye appearances and histological characters that depend upon certain modifying influences, of which the following may be enumerated as the most important:—

1. The peculiarities of the anatomical structure of the lungs.

2. The mode of origin and spread of the tubercles: whether from some pre-existing tubercular focus by way of the lymph paths or vascular channels; or by direct and primary infection of the lungs along the respiratory tract.

3. The degree of the acuteness of the process, and the stage of development in which we happen to meet with the tubercles.

In reference to the first condition, while I do not wish to dispute the doctrine laid down by some pathologists that, *miliary tubercle always begins as a proliferative growth in connective tissue,* still, I would draw attention to the limited extent of this tissue in the alveolar walls. The process has so little room for play, and its development is so rapid, that it quickly passes the boundary

line, and at once exerts an irritative influence on the alveolar epithelium, which, as we have seen, takes no small share in the formation and spread of tubercles in the lung.

From a microscopic examination of some tubercles, it would be impossible to say how they had originated, whether within or without the alveolar wall. We must be guided by the processes that are going on in the alveoli between and around the tubercles. My own limited observations caution me against drawing any hard and fast line on the point, and also teach me to be on my guard lest any fallacy in histological descriptions should creep in from one's imagination.

We have now to pass on to the consideration of the forms of miliary tuberculosis that are localised in the lung and run altogether a more chronic course, viz. :—

1. Partial disseminated miliary tubercle, and
2. Localised primary tuberculosis.

The first occurs more frequently in children than in adults. The lesion is not, like the acute miliary form, uniformly distributed in both lungs. Usually one lung is affected, and even in this the tubercles are by no means uniform in their distribution, but generally limited to a part of a lobe. The unaffected parts of the lung may look quite normal, or at most perhaps a little congested.

The arrangement of the tubercles is quite typical: they appear in the form of miliary or submiliary greyish granulations *grouped around a relatively large caseous focus situated either in the lung parenchyma itself, or immediately outside it as for example in the bronchial glands.* So far as my own experience is concerned, I do not remember to have seen more than one case where only one lung was affected, and it occurred in a child about three years of age that died from burns. There were two patches of caseous pneumonia, abutting on the pleural

surface of the lower lobe of the left lung, and spreading from them, towards the central parts of the lung a zone—like eruption of miliary tubercles. Those nearer the caseous pneumonic focus were more closely set, while those further away were scattered and more discrete. The bronchial glands corresponding to the lung were caseous and a few tubercles were found in the upper lobe. The right lung was congested—the result of the burns—but was quite free from tubercular disease. On the other hand I have pretty frequently met with a caseous pneumonia, pretty extensive in one lung, and found in the other lung a combination of lobular caseous pneumonia with miliary tubercle. Such cases lead us at once into the domain of pulmonary phthisis.

So also the second variety, localised primary tubercle of the lung, which is an example of a primary tubercular process occurring in the lung and spreading mostly along the ramifications of the smaller bronchi ; it represents one variety of tubercular phthisis. It is seldom met with in this pure form, but more often associated with other morbid changes, and I will therefore defer its consideration to the next lecture on tubercular pulmonary phthisis.

LECTURE III.

In passing on now to the subject of tubercular pulmonary phthisis, I am conscious of entering a field of inquiry so wide, and yet so thoroughly explored during the last decade by physicians, pathologists, and also by staticians, that the art and science of discovery almost seems to have been exhausted. In fact, the field seems closed to all but the therapeutist, who stands alone in possession of it, with the prospect still before him of a brilliant achievement in the discovery of some remedy, prophylactic or otherwise, that will effectually arrest the ravages of one of the direst diseases which flesh is heir to.

With regard to its pathological aspects—excepting reference to my own limited experience, which I may perhaps be allowed to add to the common stock, and to utilise in my endeavour to elucidate the subject—I cannot pretend to give you anything that is new or original in contrast to what is already known and recorded by accepted authorities on the subject; and this lecture will, therefore, consist mainly of a review of the more important facts relating to the pathology of the disease.

First of all, you will no doubt expect to hear what remarks I have to make concerning its etiology; it is unquestionably a most important part of its pathology,

and a subject about which much diversity of opinion still prevails. At the same time it is a subject far too complicated and extensive in its relations to admit of anything approaching adequate treatment in the time and space I have at my disposal for this lecture, and I must therefore ask you to excuse my going into it further than touching upon the more important points connected with it. (31)

During what we might term the pre-microscopic period, when the views of Laennec and his followers held sway, a much debated point was the relationship of inflammation to the tubercular lesions in phthisis. With their leanings towards the ancient humoral pathology, they strenuously denied the participation of inflammatory processes in the production of phthisis, and though they admitted their existence, they looked upon them as incidental complications that had nothing whatever to do with the development of tubercle. As I have mentioned in a former lecture, such views were shown by Addison and Virchow to be erroneous, and the result of imperfect methods of investigation. These two revolutionists taught the phenomenon underlying *all* phthisical processes was essentially inflammatory in its nature, but that the inflammation was distinguished by certain peculiarities, which they regarded as specific, and accordingly named it scrofulous or caseous pneumonia. (32). Niemeyer (33) attempted to simplify matters by robbing the inflammatory process of these specific characters ascribed to it by Addison and Virchow. According to Niemeyer, the consolidation and destruction of the lungs, which form the anatomical basis for consumption, are usually the products of a *simple chronic catarrhal pneumonia*, the tendency of which to terminate in caseation is to be explained partly by the chemistry of the process, and partly also by some inherent weakness of constitution in the individuals attacked. This

caseation ought not to be viewed as tubercle, but rather as a preparation of the soil for its development, which, in by far the great majority of cases of tubercular phthisis, is a secondary phenomenon. Thus, the teaching of Laennec gradually fell into the back ground as that of Niemeyer rapidly gained many adherents.

The artificial production of tubercle in animals by Villemin and others (34) in 1865 diverted the current of thought in an entirely new direction, in which it continued to travel, until the culminating point of interest in the etiology of the disease was reached by Koch's discovery of the bacillus. And this organism is still the centre of attraction around which scientific opinion has ever since been oscillating concerning its actual etiological significance, and its exact relationship to tubercular disease. Koch demonstrated the constant presence of the bacillus in the sputum and in the tubercular lesions in a series of 29 cases of pulmonary phthisis. Such investigations have from time to time been repeated, and Koch's results confirmed over and over again by physicians and pathologists in all parts of the world, so that, nowadays, in no case of phthisis is the diagnosis complete without an examination of the sputum for bacilli in order to determine its tubercular character. Neither is the post-mortem record of a case completed unless the pursuit of the bacillus is continued and carriod to its favourite haunts in the pulmonary tissue. As one of the many in Berlin who witnessed the Koch treatment in phthisis, I have a lively recollection of the extent to which the detection of the bacillus in sputum was practised as a diagnostic procedure, and of the importance attached to it by the believers in the infective and specific nature of the tubercle and in a bacillary form of pulmonary phthisis.

Now, just as Laennec and his followers made casoous material the anatomical basis for his doctrino of the

unity of phthisis, binding all forms in which the material was present under the term tubercular, so Koch and his followers assume a like position for bacillus as the etiological factor for establishing the identity of all forms of tubercular diseases of the lungs (acute and chronic), and for the unification of tubercular disease generally. His doctrine teaches that the bacillus is the cause of the disease, whatever be its exact pathological nature and the variations in its anatomical structure.

Such views at first naturally aroused adverse criticism, and for the first year or so following their promulgation, they were hotly discussed, and the "pros" and "cons" keenly argued by the bacteriologists on the one side and the pathological anatomists on the other. (35)

The literature of the subject is much too scattered and much too extensive to give even an epitome of it here, but I think I shall not be wrong in stating, after taking into consideration the relative position of opinion at the present time that the balance has gradually increased in favour of Koch's views, and that notwithstanding a few notable exceptions, there is a distinct majority not only supporting the view of tubercular phthisis as a specific disease, to which the bacillus stands in direct causal relationship, but even maintaining the identity of all forms of tubercular processes in the lungs on this common etiological basis. These views are now taught in some of our modern text-books on pathology (Green, Hamilton, Payne). On the other hand in the later editions of some of our well-known text-books on medicine, where the results of clinical observation have to be compared with the hard facts of post-mortem room experience, they are accepted with a considerable degree of reservation, particularly those relating to the identity of such affections as acute miliary tuberculosis and pulmonary phthisis (Bristowe, Roberts, Fagge).

Amongst more recent contributions, there is one by

Dr. Cornet, a former pupil of Koch and a staunch supporter of his teaching, which deserves special mention.

Cornet undertook a series of exceptionally laborious investigations, which extended over several years, to determine the presence and the distribution of the tubercle bacillus outside the body in the most varied localities.

He directed his attention to public places and establishments of all sorts wherever human beings congregated, particularly to hospitals, asylums, barracks, prisons, to places of amusement and public resort, such as theatres, concert-halls, restaurants, to business establishments, and lastly to sick rooms in private houses where patients lay ill from phthisis. In these places he collected from the walls, floors, and in hospitals and sick rooms from the bedsteads and various articles of furniture and clothing, accumulations of dust and dirt, of which he made an infusion in sterilised broth, and then injected this into guinea pigs. Every precaution was taken to obtain young and healthy animals, and to isolate the injected ones from those for control experiments. The outcome of his observations would seem to show, *that the most dangerous focus for the spread of tubercular disease amongst human beings is man himself*, but that it is *the sputum* and *not the breath* of phthisical individuals that furnishes the bacilli. Moreover, as regards the risks of infection, everything depends on the methods adopted for disposing of the tubercular sputum. So long as it is kept in a moist condition the dangers of infection are minimal, but if it be allowed to dry and to contaminate the atmosphere in a pulverised form, the danger of infection is increased tenfold. In all public institutions where these precautions in respect to the sputum were not observed, and in the sick rooms of private houses where the habits of the patient and household were not cleanly, where, for instance, the patient spat about

on the floor or into handkerchiefs, so that the sputum became dried, then the infusions of the dust, &c., collected, yielded by far the most successful results in the inoculation experiments on the guinea pigs, of which a large proportion became infected with tuberculosis.

The interest which the experiments possess in reference to the etiology of tubercular pulmonary phthisis, is the support they give to the theory of its production by the inhalation of the bacilli, in which, of course, the respiratory tract plays the most important *rôle* as the channels of infection. They show, too, that the tubercle bacillus is not "ubiquitous" within the meaning of the term as hitherto supposed. Cornet looks upon phthisis as much on infectious disease as typhus, scarlet fever, or diphtheria; he is decidedly not inclined to accept the so-called "constitutional predisposition," or "tissue proclivity" to tubercular disease as an etiological factor of much importance, though he would not deny that such a disposition might be acquired as the effects of some previous disease, or as the accompaniment of unfavourable surroundings. The reason why some are attacked with tubercular phthisis and others escape it is to be referred to the doctrine of chances, just in the same way as those who happen in warfare to become victims to the bullets of the enemy.

Baumgarten argues even more strongly against the existence of a "constitutional predisposition," which, he says, is purely a gratituous assumption, and not based upon actual proof.

According to Baumgarten *the most important factor* of all in the etiology of tubercular disease, and especially phthisis, is *hereditary transmission*, by which is implied the *transmission of the virus itself* and *not* of a "tissue predisposition" to its influence; moreover, this transmission is effected during intrauterine life mostly direct

from the mother through the placental circulation. (36) The number of cases where the disease has been acquired by the accident of injection from without is, according to Baumgarten, comparatively small compared to the number of cases traceable to hereditary influence.

The tubercular virus thus implanted in the organism, may either manifest itself in congenital disease, or break out in the earlier years of life, or it may remain latent during the entire life of the individual to become handed down to posterity and produce disease in future generations. Tubercle bacilli that have gained access either directly or indirectly into the fœtal circulation, must necessarily, according to physiological laws, first become deposited in certain organs or tissues, amongst which the lymphatic glands and the bone marrow take the first place.

Here they remain latent and kept in abeyance by the vital energy of the growing embryonic tissue, until under certain favourable circumstances, such as predominance in their number or in the degree of their innate proliferative activity, the accession of such extrinsic or accidental complications as inflammations or injuries, weakening the vitality of the tissue—they are able to overcome the tissue resistance and call forth tubercular disease of glands and bones.

In this way are to be explained the instances of congenital tubercular disease occurring from the first week to the first month of extra-uterine life, as well as its later manifestations in glands, bones, and joints, which structures Baumgarten believes, are more frequently the primary seats of tubercular disease than the lungs, although, it must be admitted, there are no positive or complete statistics showing the relations between them in this respect.

He insists particularly on the extreme chronicity of tubercular disease, on its insidious progress and its

peculiar latent tendencies as distinguishing features, and considers that as an hereditary affection it is analogous in every respect to syphilis, but especially in this, viz., that it is the virus itself in the form of the bacilli or their spores which is transmitted, and that there is no such thing as a transference of the so-called tubercular diathesis or predisposition.

Coming now to cases of tubercular disease, especially tubercular pulmonary phthisis, which owe their origin to accidental cases, such as infection from without, we have already alluded to Cornet's experiments and will here refer to his opinions based upon them,—opinions shared by many others. Cornet maintains that tubercular disease of the lungs in the form of pulmonary phthisis is for the most part a primary affection, and that it is caused by the inhalation of an atmosphere contaminated with the bacilli or their spores. Accordingly the bronchial ramifications are the channels through which the infection takes place.

While not wishing to infer that no bacilli enter the lungs with the air stream, or that there is no such event as an inhalation-tuberculosis in man, Baumgarten, notwithstanding the frequency with which the lungs are found to be affected, expresses himself in favour of its hæmatogenous origin in the majority of cases, effected indirectly through the lymphatics from a latent focus somewhere in the body. The only explanation he gives why the lungs are so often affected is based upon the results of his numerous inoculation experiments, which show that, whatever the method of infection, they are pre-eminently the favourite places for the manifestation of the disease.

Against Cornet's views he advances the negative evidence from similar experimental investigations conducted by Bollinger, Celli, Gaurnieri, Mendelsohn, Pernice and Santa Sirene. He states, moreover, as the results of

years of personal observation and experiment that certain parts of the body, viz., the skin, external mucous membranes, and the lungs in particular are peculiarly resistant to the invasion of microbes on account of the natural protection afforded by their epithelial covering. The ciliated epithelium of the upper naso-respiratory tract is constantly engaged in casting out all kinds of foreign particles, and only injuries of a serious nature can break down its natural protective influence.

Of all the natural channels through which accidental infection may occur, the gastro-intestinal tract is the one that claims special attention, for the intestinal mucous membrane appears to be peculiarly defencelesss against bacterial invasion.

Still, even here, two most important points must be borne in mind as regards the effects of bacillary invasion, viz., the number of bacilli introduced, and the degree of their virulence. Like other pathogenic organisms tubercle bacilli exhibit variations in the degree of their virulence which is attenuated by transmission through the bodies of various animal species, and hence, according to Baumgarten, the dangers arising from the consumption of tuberculous meat and milk (especially the latter) have been somewhat overrated. No doubt cumulative effects may arise by long continued consumption of such food; but, for all that, Baumgarten is not inclined to attribute to the gastro-intestinal tract much importance as a channel of infection on account of the ineffectiveness of the causes operating through them. (37)

So far we have examined the views of those who agree in the main principle, but differ concerning the details of its application. In other words, they all regard tuberculosis as a specific disease to be referred to the operation of a specific virus—the bacilli; but they are not agreed as to the mode and sphere of the action of the virus. Amongst those antagonistic to Koch's doctrine, two of

the most uncompromising opponents are Drs. Heanage Gibbes and Shurly, whose labours are not yet completed; only the first instalment has appeared in print (vide under No. 35 ref.), and this seems to be mainly a critical digest of the opinions of the various clinicists and pathologists on the subject up to the present time. From a perusal of it, it is quite clear that Drs. Gibbes and Shurly are not believers in the doctrine of the unity of phthisis and tuberculosis, based upon the bacillus as the etiological factor, and accordingly, from this standpoint, they cannot subscribe to the view of the specific and infective nature of tubercle; on the contrary, they maintain that the causal relationship of the bacillus to the various forms of tubercular phthisis has not yet been sufficiently established; and they incline to regard its presence in the lesions as an effect rather than as the cause. Dr. Gibbes attaches great importance to the histological analysis of tubercle as the only reliable method of determining its distinctive characters. But they inform us *that a series of experimental investigations are still in progress*, by the results of which they hope to prove the correctness of their convictions.

Now herein lies, it seems to me, the weak point in their arguments. To start with a certain conviction or bias, the value of which as a scientific evidence brought forward to upset a theory, remains to be proved by experimental investigations not yet completed, is a method of procedure open at least to criticism if not to fallacy.

Well may you exclaim "When pathologists of such repute differ, who is to decide?" Now in reviewing the opinions of the numerous authorities quoted, one or two points have struck me as being worthy of comment. First of all, it appears to me that the pure pathologists, especially those among our foreign brethren, show a tendency in their observations to look at the question

too much through the spectacles of experimental research; they are inclined to appeal to experiments on animals for the explanation of many knotty points arising in the pathology of the disease as affecting human beings.

The conditions modifying the disease induced in animals by direct experiment must differ materially from those influencing the disease as it occurs idiopathically in man. In the former case the experimenter has them entirely under his control, while in the latter case they have to be sought for and linked into evidence from the clinical history of the case; and accordingly each individual case has to be judged of according to its own peculiar merits. I do not wish it to be inferred that I am insensible of the great value and importance of experimental pathology, or of our indebtedness to it for the elucidation of many points in the pathology of diseases affecting the human race. But I have long held the opinion that pathological inquiry into human ailments coming daily under our cognisance as practitioners of our art, when divorced from clinical knowledge and experience is, in a sense, narrow and one-sided, compared with pathological inquiry in the post-mortem room that goes hand in hand with clinical observation. The value of this co-operation is seen in the writings of some of our well-known pathologists (38) and is nowhere better illustrated than in the posthumous and monumental work of one of the most brilliant clinicians and pathologists of modern times, (39) whose untimely death those that had the advantage of profiting by his teaching will never cease to lament.

As regards my own opinions concerning tuberculosis and tubercular phthisis, I am a firm believer in Koch's teaching, (40) and as one of the many who witnessed his methods of research, and further had the advantage of working in bacteriology in the hygienic institute in

Berlin under the supervision of his able assistants, I could not arrive at any other conclusion, however sceptical my ideas were when I first began. Moreover, the results of Koch's researches have since received such wide confirmation by unbiassed investigators working on the same lines, that I may safely repeat the statement that I made at the commencement of this lecture, when I said, that after taking into consideration the relative position of opinion at the present time, the balance has gradually and largely increased in favour of Koch's views.

But I cannot agree with Baumgarten and Cornet who would strike out "constitutional predisposition" from the category of the etiological factors of tubercular disease in general, and pulmonary tubercular phthisis in particular, who deny or douht its existence, because they believe it does not stand the test of direct proof. Such experienced pathologists as Orth, Ziegler, Birch-Hirschfeld and others, all of whom are believers in the pathogenic causal relationship of the tubercle bacillus, still maintain that constitutional predisposition is an important element in the etiology of tubercular disease that has to be reckoned with. Neither do I endorse Baumgarten's extraordinary views about the lungs as channels for primary infection. Both clinical experience as well as pathological examination of the numerous instances of the disease in man, render it very difficult to accept the proposition that by far the greater number of cases of pulmonary tubercular phthisis are not of primary origin, but are local manifestations, secondary and traceable to some pre-existing latent focus of disease somewhere or other in the body, and consequently are the results of hæmatogenous infection.

Nay, I even believe that not a few instances can be cited, where the pulmonary affection at its commencement was not tubercular at all, but in all probability

simply of an inflammatory nature, and that it became subsequently stamped with the tubercular characters by the lodgment of the tubercular virus conveyed through the respiratory tract. Accordingly, I consider Cornet's experimental investigations constitute an important contribution to the bacillary origin of tubercular pulmonary phthisis of much value and interest to the practical physician.

I must apologise for taking up so much of your attention with the subject of the etiology of tubercular disease ; but I have taken the opportunity at this stage of my lectures to enter at length into the discussion of it, and to lay before you some of the most recent work done in this direction, chiefly on account of its important bearing on that form of the disease now under consideration, viz., Pulmonary Tubercular Phthisis.

In my next lecture I shall turn to my own series of cases, discuss its association with, and relationship to, other diseases, and describe the morbid anatomy and histology of its various forms.

Postscript.—Amongst experimental researches of recent date bearing on the chemical aspects of pathological investigation, and particularly on the *modus operandi* of the Koch treatment, those of Professor Maffucci (41) are of such exceptional interest that I cannot omit a reference to them. Maffucci took pure cultures of the tubercle bacillus in solid glycerinated blood serum or in fluid blood serum from one to six months old, *sterilised them completely*, so as to effectually destroy the vegetative vitality of the bacilli, and then injected guinea pigs with the sterilised products.

After a period varying from three weeks to four months following the operation, all the animals died of a febrile disorder terminating in general marasmus. Examination of the organs after death showed marked atrophy of the cell elements, blood stasis, and in a few

instances simple catarrhal inflammation, *but without the slightest evidence of the development of tubercular lesions.*

Hence it would appear that the action of the bacilli is twofold, viz., a mechanical one producing morphological disturbances in originating certain tissue lesions; and a chemical one, arising from the metabolism between the bacilli and the tissues, and producing certain chemical substances allied to the toxalbumins, to the operation of which the leading constitutional symptoms of tubercular disease (especially phthisis) such as pyrexia, anæmia, and wasting may be referred.

The absence in these cases of tubercular lesions appears to me to afford the strongest possible evidence in favour of the bacillary theory.

The temperature employed in the operation of sterilisation was sufficient to destroy the vitality of the bacilli, but it in no way interfered with the poisonous chemical products resulting from their growths in the nutrient media.

LECTURE IV.

In the morbid anatomy and histology of pulmonary tubercular phthisis, there are at least two essential and distinguishing features to be more or less constantly kept in view, viz., the specific nature and destructive tendencies of the morbid process, as suggested in the terms employed to describe the disease. Another important element in the anatomical changes, which is often contemporaneous with the destruction of the pulmonary tissue, is the occurrence of a reactive inflammation resulting in the production of new fibrous tissue to replace the loss ; this compensatory process, which is an expression of nature's restorative efforts, plays a most important part in the more chronic cases. If, in accordance with modern pathological teaching, we define tubercle as the result of an inflammatory process of a *special* productive type, we shall find it at all events in most cases of phthisis, so intimately associated with other pathological processes taking place in the lungs, especially with simple inflammation of an exudative or proliferative character, that the morbid anatomy of the disease becomes an exceedingly complex subject, including a number of different pathological phenomena. In almost every case we shall find the inflammatory neoplasm known as tubercle combined in variable extent with pneumonic processes of different types ; at one part the tubercle is in the midst of alveoli filled with an exuda-

tion resembling that in fibrinous pneumonia ; in another part the alveoli between and around the tubercles are affected with a catarrhal inflammation, and their contents are mainly cellular, resembling the exudation characteristic of catarrhal pneumonia ; or, as is most frequently the case, the exudation consists of a more or less homogeneous or caseous material, and the alveolar walls, as well as the general fibrous framework of the lungs are thickened by cellular infiltration and swollen with inflammatory œdema.

Accordingly then we may briefly express the entire morbid process by the following equation :—

The different forms of pneumonia in varied combination—fibrinous, catarrhal, caseous, and interstitial, *plus* tubercle = pulmonary tubercular phthisis.

Now the important problem underlying all this, is to determine the relation between these quantities so as to arrange them in their proper sequence. In other words we must ask ourselves the following questions :—

Is the development of tubercle in every case of tubercular phthisis the initial process, to which the associated pathological changes above mentioned are secondary ? or, conversely, do they precede the development of tubercle ? Thirdly, dismissing the notion of any causal connection between them, may not the different pathological processes, which collectively make up the disease, be co-ordinate with, and yet independent of, one another ?

I must admit that, merely from anatomical inspection and histological investigation, I should certainly not feel disposed to give definite answers to these questions, especially in cases where the disease was advanced.

A knowledge of the clinical history and facts may afford us material assistance in arriving at a proximate conclusion, and thus we undoubtedly meet from time to time with cases where the prelude to the establishment

of tubercular disease is represented by a pulmonary catarrh of a simple type, and the tuberculosis is to be referred to the accident of infection from without. I have now in my mind such a case, which I may quote as an example.

A finely-built policeman, of strong constitution, with no history of previous illness, and *not the slightest trace of hereditary taint*, caught an ordinary cold at a picnic on a wet day in the autumn. As a consequence he had, what he termed, a "cold on the chest" (bronchial catarrh), which compelled him to remain indoors for a few days. Feeling somewhat better, he resumed his duties, though, as he expressed it, he never seemed able to thoroughly shake off the cold, which left him with an irritating and troublesome cough. Nevertheless he continued to perform his duties; and we know the kind of places and surroundings into which a policeman's duties often take him. About *three or four months later* he found he was losing strength and beginning to lose in weight. He often felt chilly and then hot at night, and broke out into perspirations when in bed. Moreover, he became rather short of breath on exertion, his cough became more troublesome, and was accompanied by increased expectoration; and he now noticed that his sputum was often markedly tinged with blood. On one or two occasions he coughed up small quantities—about a teaspoonful—of pure bright frothy blood. He was admitted in the early part of this year into the Queen's Hospital, under the care of Dr. Suckling, with whose kind permission I have been able to observe and quote the case. Physical examination revealed pretty extensive infiltration and consolidation of one apex, and tubercle bacilli was found in considerable numbers in the sputum. He was put under a course of the Koch treatment, and improved considerably, so that in six weeks he was able to leave the hospital.

It would require a considerable stretch of imagination to suppose this man was the subject of latent tubercular disease, that was called forth into activity by the exciting causes of exposure to cold.

In children cases are well authenticated, where a broncho-pneumonia following measles or whooping-cough has preceded the development of a tubercular phthisis, and I have myself several such instances amongst my cases. On the other hand an early hæmoptysis, occurring without any noteworthy premonitory symptoms, affords us strong evidence in favour of the disease being tubercular from the outset, and of a latent and insidious nature. In such cases the individuals are mostly of delicate build and constitution, and there is usually a well-marked hereditary history.

The patient may possibly get out of breath from some extra physical exertion; he has a fit of coughing, which is immediately, and quite unexpectedly, followed by a severe attack of hæmoptysis. Should it at once prove fatal we may find at the autopsy that the hæmorrhage proceeded from a latent but fairly extensive patch of tubercular disease in the apex of one lung, the existence of which was probably not suspected; and yet degenerative changes, such as caseation and ulceration had been going on insidiously in the patch, sufficient in extent to involve a branch of the pulmonary artery and also the wall of its corresponding bronchus. Possibly a small aneurysm of the artery may be found ruptured, though this happens more frequently after the disease has been diagnosed, when hæmoptysis is a late symptom.

Now this latent apical affection represents *a localised tuberculosis*, whose origin and characters may be twofold. In the first place it may have started *directly* from the inhalation of the virus, as a tubercular bronchitis and peri-bronchitis—the so-called apical catarrh, the symptoms of which may have been so slight that the patient

did not feel the necessity of seeking medical advice before the occurrence of the hæmoptysis.

Secondly, the disease may have spread to the apex *indirectly* through the lymphatics from some *older* tubercular focus away from the lungs, and appear in the lungs as disseminated interstitial miliary tubercles (partial disseminated miliary tubercle). In both instances the development of the lesion is comparatively slow and insidious; it becomes conglomerate before retrogressive changes set in, and its further spread may for a time be hindered by a development of fibrous tissue at its periphery. Here again in its caseous stage we may meet with the difficulty already alluded to in determining the initial anatomical characters of the lesion. The discovery of an older caseous focus outside the lungs, and the presence in the peripheral fibrous tissue of clusters of greyish semitranslucent miliary granluations favour the second mode of origin just described, as an anatomically true tubercular process. (Baumgarten's indirectly hæmatogenous origin of tubercular phthisis.) What may now happen, supposing the hæmoptysis is not severe enough to kill the patient at once? One of two events: Either the development of an acute caseous pneumonia, rapidly spreading throughout the remainder of the lung, or an acute pneumonic exacerbation, gradually subsiding again into a chronic condition.

As a result of the pulmonary hæmorrhage, the fibrous barrier around the apical disease becomes partially destroyed, and the lung tissue immediately outside is the seat of patches of hæmorrhagic infiltrations (parenchymatous and interstitial); blood mingled with the caseous material containing the tubercular virus is sucked down into smaller bronchi and bronchioles in various parts of the lung, setting up a disseminated lobular pneumonia, which becomes confluent and rapidly caseates. In the first case the rapid development of the caseous pneu-

monic phthisis is the result of a sudden and widespread infection of the lung from the aspiration of the tubercular virus, rather than as the direct consequence of the pulmonary hæmorrhage. The corresponding lung, where no hæmorrhage has taken place, is usually implicated before the fatal termination occurs. It is in cases where the apical lesion bore the characters of a tubercular bronchitis and peribronchitis that I have observed this supervention of acute pneumonic phthisis. Death takes place usually within a month or two from the date of the hæmoptysis. In the second event, where the acute pneumonic exacerbation subsides into a chronic condition, we can only suppose that the lung was implicated to a less degree, and the pneumonia may perhaps be referred to the pulmonary hæmorrhage. It clears up and becomes arrested by the development of fresh fibroid and indurative changes, and represents merely a further but more limited step in the general advance of the disease. Such cases as the above are not examples of *phthisis ab hæmoptœ* as described by Niemeyer, because, as we have seen, a localised but latent phthisis actually precedes the hæmorrhage.

Now, contrasted with this example of secondary caseous pneumonia above described, we shall meet with instances where the tubercle bacilli on reaching the lungs may, from the outset, and at once generate a primary caseous broncho- or lobular pneumonia of a more chronic type, with which the subsequent development of miliary tubercles may be associated as a secondary process. In this inverse order of events in different cases lies the difficulty in the anatomical recognition and correct interpretation of the disease as a whole; for it is represented by an amalgamation of the results of tubercular with those of simple inflammation, and moreover is frequently presented to us on the post-mortem table in such an advanced condition, that it is impossible from anatomical

inspection alone to say definitely what its origin has been, whether primarily tubercular or simple inflammatory. On looking over the post-mortem records of the cases selected from a large number that have come under my personal observation in the dead-house, I can find 22, or rather more than 14 per cent. where the pulmonary affection was associated with *chronic* tubercular disease in other parts of the body, *e.g.*, bones, joints, (42) skin, mucous and serous membranes, and the genito-urinary tract.

Here we may reasonably assume that in some instances the lungs became infected secondarily by the propagation of the disease through the lymphatic system. (Baumgarten's indirect hæmatogenous origin of pulmonary tubercular phthisis.) At the same time, in other instances a different mode of origin is also conceivable, viz., a later but independent appearance of the disease in the lungs, the result of direct infection from without through the respiratory tract; for we can reasonably suppose that the resistant power of these organs in an individual already a victim of the disease is sensibly diminished, so that the respiratory system becomes extremely susceptible to the pernicious influence of the virus. It is also possible—nay, in the highest degree probable, that the disease in the lungs of some of these cases was the result of the concurrent action of both modes of infection, direct and indirect.

In another highly interesting, though much smaller group of cases (5·3 per cent.), the tubercular character was beyond all doubt engrafted upon a primary simple inflammatory affection of the lung. The analysis of this group is as follows:—

(A.) Unresolved catarrhal pneumonia, the sequence of measles and whooping-cough, in which a tubercular phthisis in an early stage of development was found.—4 cases.

(B.) Membranous laryngitis and acute lobar pneumonia with pleurisy, terminating in empyema, with much thickening of the pleura, fibroid induration of the lung and bronchiectasis, caseous pneumonia and grey racemose tubercle in an early stage.—2 cases.

(C.) Chronic pleurisy with old and greatly thickened and adherent pleura, pleurogenic interstitial pneumonia and bronchiectasis, secondary tubercular peribronchitis and interstitial tubercle.—5 cases.

In these 11 cases the tubercular disease was latent, but evidently recent, and so slight in its extent that its diagnosis during life was marked by the symptoms of the major affection.

There is yet a third and also small group, 11 in number, to which a certain amount of interest may be ascribed, in that the tubercular affection of the lung occurred in association with other diseases of an entirely different character. Here, too, the pulmonary disease was essentially chronic in its character, and, comparatively speaking, slight in its extent.

(A.) Chronic interstitial nephritis, 4 cases; in all there was chronic thickening and adhesion of the pleura; in two of them old encapsuled caseous masses were found in the apex of one lung accompanied with fibroid induration, and around them more or less recent disseminated grey tubercles (partial disseminated miliary tubercle).

(B.) Mitral stenosis—caseous tubercular bronchitis and broncho-pneumonia with cavity formation in one lung, though not extensive—a few grey miliary and caseating tubercles scattered here and there in the upper lobes of the opposite lung.—2 cases.

(C.) Chronic alcoholism (alcoholic neuritis).—2 cases.

(D.) Death from accident, where a comparatively early stage of tubercular phthisis was found at the post-mortem.—3 cases.

Excepting chronic alcoholism, which is set down

as a predisposing cause, it is conceivable that the pulmonary disease originated quite independently. In two of the cases of nephritis the tubercular disease was in part obsolescent, and probably quite as old in date as the renal disease. In the other two it is possible that it developed subsequently to the renal affection. Clinically speaking, the symptoms of the renal disease were the conspicuous features in all four cases, and though a pulmonary affection of a chronic nature was recognised, its tubercular character was not certainly diagnosed, even if it were suspected.

Now all the remaining cases may be included in one group, in which the tubercular phthisis constitutes the *primary substantive* disease that was diagnosed and treated as such. In fact, all the patients were obviously suffering from phthisis, for which they came to the hospital to be treated.

In this large series of cases, between 80 and 90 in number, all the anatomical varieties of the disease are represented, and fortunately I happen to have still in my possession a large number of histological preparations which I made from the material collected from typical examples in this as well as in the other groups I have just enumerated.

The Morbid Anatomy and Histology of Tubercular Phthisis.

It has been said with some truth that, from an anatomical point of view, no two cases of tubercular phthisis will be found exactly alike, and no doubt one explanation of this fact is that phthisis, like many other diseases, often runs an irregular course; for although the tendency in the main is a downward course from bad to worse, its progress as indicated by its symptomatology is disturbed by considerable fluctuations. Its apparent

favourable progress at one time may be suddenly interrupted by fresh exacerbations of a more or less acute character, and we may find at the post-mortem, variations in the morbid appearances corresponding with this irregularity in its clinical aspects. Still if we adopt a broad clinical classification of the disease into the (1) acute, (2) subacute, and (3) chronic varieties, we shall also find certain anatomical changes predominating in one or the other case which correspond with the clinical type of the disease and also *more or less* (43) with the physical signs noted during life.

Let us first take a case of acute phthisis, in which the duration of the disease from its onset to its fatal termination covers a period varying from a month or six weeks, to two or three months at the most. The individuals attacked are usually young subjects, and the disease in some of its clinical aspects, particularly in regard to its physical signs, resembles at first unilateral acute pneumonia implicating the upper lobe of the lung, from which, however, it soon becomes differentiated by its protracted course and by differences in the temperature curve and in other local and general signs. Basing my description of its morbid anatomy and histology on several typical cases of which I have complete notes, we shall find both lungs affected; but the one in which the disease commenced is involved to such an extent that it may be almost solidified throughout. In a young adult its weight may vary between 40 and 50 ounces. The disease is most advanced in the upper lobe, which may be found partially adherent to the thoracic wall by loose and œdematous fibro-cellular tissue, the rest of the lung is free, but its pleural surface may present patches of recent fibrinous inflammation. On making a longitudinal section through the entire lung from the middle line of the posterior border to its root, we obtain an extensive view of the lesion which presents to us without doubt the

characters of a pneumonia of a special type, viz., a rapidly extending caseous pneumonia. The cut surface has a reddish grey colour, the greyish mottling being most marked in the upper part, the darker red being the basis or predominating colour in the lower part of the lung. But *the distinguishing feature is the presence of distinct and opaque yellowish white spots and patches* which are scattered all over the cut surface. They are usually small, irregular in form with rounded margins, but here and there a few assume a trifoliate shape corresponding to the infundibula or alveolar passages. (44) Some are distinct and sharply demarcated, others pass insensibly into the reddish grey hepatisation around them. In the upper lobe we may find one or two small excavations, irregular in shape with shreddy margins caused by the disintegration of the tissue.

Thus in the lung where the disease is most advanced we have to do with a pneumonia that is quite lobar in its distribution. In the corresponding lung where it is in an earlier stage of development we see the lobular characters of its distribution well defined, especially in the upper lobe, where the pneumonic foci are scattered in the pulmonary tissue as roundish nodules or nodes. Some of them reach the pleural surface, on which they project, and can be felt as distinct lumps. They vary in diameter from one-eighth to five-eighths of an inch, and on section are of a reddish gray colour, and the larger frequently show an opaque yellowish white centre. In consistence they are firm but frangible; the cut surface has a well marked granular, but a peculiarly dry appearance; in fact, with the exception of their opaque yellowish centres, the larger nodules represent a hepatisation intermediate to the red and grey stages of an ordinary croupous pneumonia.

In the very acute cases interstitial changes are scarcely recognisable with the naked eye, except perhaps

in the upper lobe of the lung most extensively involved ; there a few œdematous looking, pinkish grey strands of thickened interstitial tissue may be seen on close inspection in the hepatised parenchyma.

Towards the base of the less affected lung the lesions become still smaller and more scattered. Here they are, in fact, small foci of tubercular bronchitis and peribronchitis, in which a few of the surrounding alveoli become involved; and they correspond to that variety described in some text books as soft, grey, or early yellow tubercle. Thus in one and the same case, we have seen all the varieties of caseous pneumonia described by some authorities, viz , lobar, lobular, and broncho-pneumonic. I must not omit to mention that the occurrence of a primary lobar form has been called in question by some pathologists, who do not believe that an entire lobe or a great part of it can be all at once attacked by caseous pneumonia; they hold that the disease appears first in a lobular form, and subsequently becomes lobar by simple extension and confluence.

Passing now to the *histology* of the disease, let us examine :—

(1) a distinct opaque yellow patch ;

(2) the reddish grey hepatisation around it, or that of one of the smaller lobular foci ;

(3) and lastly, let us take one of the smallest foci last described, *i.e.*, tubercular peri-bronchitis, or broncho-pneumonia.

In (1) we have typically represented the caseating process ; all we can make out with a low power are the mere outlines of a number of alveoli, every one being filled with the same sort of material. In the centre or thereabouts we may perhaps be able just to distinguish the outlines of an intra-lobular bronchus, in which the material is breaking up into fragments. Under a higher power all structural details of the bronchial and alveolar

walls are lost, (45) and the exudation within them appears to be quite homogeneous; in some alveoli it is composed of a coarsely reticulated glassy substance, the fibrin and the disintegrating cells having degenerated into a coagulative necrosis; in others it is more or less opaque and granular; nuclei and their nucleolar remains, deeply stained, and numbers of highly refractive fatty granules are scattered amongst it, and tubercle bacilli isolated or in small masses are here and there visible in the field of the microscope.

(2) In the more recently hepatised parts the structural details come more clearly into view. The alveolar walls look somewhat thickened, and are infiltrated here and there with lymphoid cells and a few red blood corpuscles; sometimes capillary vessels filled with red blood corpuscles are seen coursing in them. With regard to the intra-alveolar exudation, *the variability in its composition is one of the distinctive features of the pneumonic inflammation.* In a number of the alveoli situated at some distance from the caseous part, *a certain amount of coarse fibrin*, entangling in its meshes a few red and white blood corpuscles, *is a constant element*, and it indicates the exudative character of the inflammation. But the predominating cellular elements in the exudation are large roundish or polyhedral and coarsely granular cells, the offspring of the alveolar epithelium, which may sometimes be seen sprouting or budding from the alveolar wall. In some alveoli the exudation is entirely composed of them, and here we have an indication of an inflammation proliferative in character (catarrhal pneumonia). Many are binucleated, others are beginning to disintegrate and contain fatty molecules. In the alveoli nearest to the caseating part the exudation is commencing to degenerate and to melt down into a homogeneous glassy-like material (coagulative necroses). Tubercle bacilli are also mingled with the exudation.

Quite exceptionally we may meet with an anatomically tubercular formation, *i.e.*, a reticular giant-celled granulation. But in this acute form of caseous pneumonic phthisis their occurrence is so seldom that we may look through many fields of the microscope before finding one.

(3) Taking next one of the smaller foci, which are scattered in a more or less discrete fashion towards the base of the less extensively affected lung, we find on microscopic examination a repetition of the histological changes, only limited within a much smaller area.

In the centre is a small bronchus cut across transversely or obliquely as the case may be; its epithelial lining may have entirely disappeared, or be only partially preserved; its lumen is occupied with a caseous detritus; its wall perhaps a little thickened by cellular infiltration, or, as is more frequently the case, partly effaced by the degenerative changes taking place in and around it. Those alveoli grouped immediately around it contain a similar caseo-cellular exudation, and their walls are somewhat blurred; only in a few quite at the periphery are structural details clearly defined; in them the exudation is fibrinous and cellular, but the proliferated alveolar epithelial cells predominate.

Histological examination of a *small conglomeration*, shows a *somewhat larger* bronchus as the centre piece, with a proliferating epithelial lining and cellular contents. Grouped around it are the separate nodules of tubercular bronchiolitis, or *infundibulitis*, if one dare coin such a term, for the centre of each little nodule is formed by either a bronchiole or an alveolar passage (infundibulum) which is stuffed with a caseous and cellular material, while in the group of alveoli belonging to it the exudation is more cellular in character. The term which Powell (46) uses to designate the entire process, *broncho-alveolitis*, is a very graphic and intelligible one. By

others it is called tubercular bronchitis, peri-bronchitis, or simply broncho-pneumonia, at all events we shall find it to be the predominating lesion in most cases of phthisis.

Such then is the histology of the most acute form of pneumonia phthisis, the "phthisis florida" of German, and "galloping consumption" of English, authors. Its essential features are, (1) the retrogressive changes that accompany and almost go hand in hand with the pneumonic infiltration; (2) the variable characters of the intra-alveolar exudation, and the invariable presence of tubercle bacilli, which distinguish it from ordinary fibrinous and catarrhal pneumonia.

An interesting question is what causes the caseation. Some refer it to the obliteration of the pulmonary vessels by the interstitial changes in the alveolar walls, and by the endarteritis of smaller branches of the pulmonary artery,—changes we shall notice pretty frequent in the more chronic forms of phthisis. Then, again, in these acute cases we are considering where such interstitial changes are much less prominent, it has been suggested that the pressure exerted by the alveolar exudation may operate as a cause. But this explanation can scarcely hold good, else how do we account for the absence of similar extensive retrogressive changes in acute fibrinous and catarrhal pneumonia. Lastly, the caseous metamorphosis has been attributed to the operation of the tubercle bacilli. In this caseous tracts where interstitial changes are absent, this explanation is, I think, the correct one.

In the next case of caseous pneumonic phthisis, which lasted between nine and ten months, *we find the caseous infiltrations invested with a zone of young proliferating connective tissue, in which the development of the giant celled reticular tubercle is a conspicuous feature.* The pleuritic adhesions were more extensive and firmer in character. In the most extensively affected lung a large

cavity was found in the upper lobe. The rest of the lobe together with a great part of the lower was solidified by tracts of caseous pneumonia *coalescing one with another through the medium of a greyish translucent connective tissue.* This large area of consolidation was riddled with small cavities. The base of the lung was œrated, but infiltrated with smaller nodules and soft grey and yellow tubercles.

The upper lobe of the corresponding lung contained isolated nodes of caseous pneumonia, several breaking down centrally to form cavities; towards the base the tubercular infiltration was more discrete and smaller, viz., soft grey and yellow granulations. The microscope showed the caseous portion of even these isolated smaller infiltrations, ensheathed by a connective tissue zone, in which all trace of the alveoli was lost. Here and there one found a minute point, which microscopical examination demonstrated to be an intra-alveolar formation of giant celled tubercle. Thus in this case all the varieties of tubercle were represented.

I have observed another curious and interesting fact in connection with those cases of pneumonic phthisis *where the right lung happened to be the most affected one:* viz., while the lesions in the upper and lower lobes were mostly large and pneumonic in character, those of the *middle lobe were all of them miliary, consisting in an infiltration of the small firm grey miliary tubercle, either discrete or conglomerate.* These small shot-like granulations are histologically made up of giant-celled systems surrounded by a well-defined reticular or adenoid zone. You will perhaps recollect that this variety constituted the pulmonary lesion in some of the cases of general miliary tuberculosis described in the second lecture. In tubercular phthisis they are met with chiefly in the more chronic cases, where they are secondary and described as interstitial tubercle (Hamilton). We shall

find them distributed also in the lower lobes towards the bases, but their occurrence in the middle lobe of the right lung has, in my experience, been so constant, that I have made a special note of the fact. Passing now to cases of pneumonic phthisis, where the duration of life was even more prolonged, and the disease in consequence more chronic in character, we shall find the fibroid changes more pronounced, and extensive and cavity formation more frequent.

Thus the upper lobe of the lung first affected may be considerably contracted and the seat of multiple excavations. Some of them are the result of bronchiectasis in combination with caseous degeneration of the walls; others proceed from the central softening and disintegration taking place in the parts affected with the caseous pneumonia, in which the exudation, the alveolar walls and connective tissue are all involved. The rest of the lung and also the corresponding one, but to a less degree, show pathological changes, for the most part tubercular in character but varying in form; thus we find, in combination, the larger foci of pneumonic infiltration, the smaller ones consisting in caseous bronchitis with peribronchitis and pneumonia (soft grey and yellow tubercle), interstitial changes with the development of interstitial tubercle (grey miliary). I have a case which I should like specially to bring to your notice, because it illustrates well the changeable course of some of the more chronic cases and also demonstrates the corresponding diversity of the pathological changes. The patient had four or five years ago an acute attack of pneumonic phthisis affecting the right upper lobe. This subsided, but afterwards, he had several intercurrent attacks in which an extension of the disease was noted every time. These secondary attacks were usually followed by an interval during which the health of the patient had comparatively improved, and his hopes of

recovery revived. Five months ago, fresh pulmonary mischief appeared, and from that date he gradually got worse up to the time of his death.

At the post-mortem the right lung was bound down to the thoracic wall by firm pleuritic adhesions. The upper third of the superior lobe was converted into a multilocular cavity, the roof of which was torn away and left in the thorax on removing the lung. The rest of the lobe was *much contracted*, and on section contained several smaller cavities, the result of bronchiectasis. The inner surface of the large cavity was naturally uneven from the presence of thickened bands of tissue intersecting it and running it in walls like fluted columns. Here and there a patch of caseous detritus adhered to the lining, which for the most part was smooth. *Caseous patches were embedded in the dense, indurated tissue between the bronchiectic cavities in the lower portion.* The upper part of the inferior lobe was completely hepatised by albumoid and caseous infiltration and riddled, with small cavities, while the lower half down to the base contained isolated lobular patches of caseous pneumonia, and smaller infiltrations of soft grey and yellow tubercle. *The middle lobe was infiltrated throughout with conglomerate and discrete firm grey miliary tubercles* (interstitial tubercle).

Left Lung, upper lobe, almost solid, riddled with small cavities, the intervening lung tissue hepatised with caseous pneumonic foci, in other places collapse and carnefication of the lung. Lower lobe crepitant, but congested, and infiltrated sparsely with firm grey miliary tubercle, quite shot-like to the feel, and with little or no tendency to caseate. In this case we have nearly every variety of tubercle combined with chronic indurative inflammation, corresponding with the acute character of the primary and intercurrent attacks, and with the chronic but insidious progress of the disease during the

intervals of apparent improvement in the patient's general health.

The above case and those similar in character which I have described before it are examples of an arrested caseous pneumonia subsequently pursuing a more chronic course, and associated with varying degrees of fibroid change. By some authorities they are classed under fibroid phthisis. But with this I cannot entirely agree, because the extent of the tubercular changes is much greater than what we shall meet with in true fibroid phthisis.

The next and perhaps the commonest variety of tubercular phthisis is that, where the disease has been *mainly the result of the inhalation of the virus in small but repeated doses, distributed at various spots in the lung relatively speaking wide apart from one another.* The disease may be an extension from a primary caseous focus in the lung itself, or from caseous bronchial glands, *with which one or more larger bronchi happen to be in direct communication.* Into the terminal ramifications of these bronchi the virus is *aspirated,* and originates, more or less simultaneously, a number of individually distinct and independent focal lesions, which at first, on account of the smallness of their size, and their general naked-eye appearances resemble very much miliary tubercles. If, however, we accept the pathological anatomist's definition of miliary tubercle, we shall find them possessing a totally different structure.

Of course, it is only in the earlier stages when the disease is localised at the apex or in the upper lobe of the lung, that we can satisfactorily study the development and the anatomical characters of these lesions. For, at a later stage, when the disease has perhaps been steadily progressing for a year or two, the anatomical changes become so varied and complex, that the most experienced pathologist will, in some cases, rather leave it an open

question than commit himself to a definite opinion as to the mode in which the disease originated, as well as to the precise nature of the initial lesions. In some of these advanced cases there are certain leading features that will guide him in forming an opinion. For instance, there may be evidences of the *uninterrupted progress* of the disease, and then an examination of the more recent lesions in the lung least affected is, I think, a fair criterion as to the character of the primary pathological changes. In a few cases where death was due to accidental or other causes I happened to meet with this variety of phthisis in the early stages of its development, and I found at the apex of one lung, or scattered throughout a great part of the upper lobe, a number of disseminated tubercular lesions which I took to be miliary tubercles, and so regarded the affection as *a localised miliary tuberculosis.* In three of the cases, however, I failed to discover any trace whatever of a primary caseous focus to fit in with the generally accepted theory of the etiology of the disease, and I therefore kept material from all three for microscopical investigation, the result of which showed me that the greater number of the lesions were *anatomically* speaking *not miliary tubercle*, though, from an etiological point of view, they were all "*tubercular*," since they all contained tubercle bacilli. Another point of importance which is clearly illustrated in these cases is that the variety of tubercular phthisis we are now considering can, in the absence of an old caseous focus in connection with the bronchial tract, arise as the direct consequence of the inhalation of the bacilli from without. We may suppose the pre-existence of excoriations or injuries of the bronchial mucous membrane, but whether this be so or not, the disease begins at different points in a certain area of lung tissue as small foci of tubercular broncho-pneumonia. Concerning the anatomical characters of the lesions in these earlier cases :—

(1) The discrete are all small, though not all of the same size. The larger vary from 1-20th to 1-10th inch. in diameter. All from 1-12th inch in diameter and upwards are distinctly opaque and caseous in the centre ; when viewed through an ordinary or simple magnifying glass pin-hole apertures are seen situated often to one side of them, and these under a low power of the microscope are found to be sections of small bronchi. In the smaller foci, 1-20th to 1-25th inch or so in diameter, the caseous centre corresponds with a bronchiole or its infundibular expansion, which is filled with caseous material ; the rest of it consists of a zone of imperfect nucleated fibrous tissue, and then outside this a number of alveoli filled with a cellular caseous exudation. A prominent feature is the extensive thickening of the interalveolar septa by an adenoid cellular tissue. Now, the smallest of all, namely, those measuring from 1-100th to 1-50th of an inch are greyish, but homogeneous and semi-translucent points which are disposed in the adventitia of blood vessels and at the margins of the interlobular septa. They are anatomically true tubercles (reticular giant-celled), and are evidently of recent and secondary origin, developing along the course of the lymphatics in the perivascular and interlobular tissue. Some of the larger ones of this variety are found immediately beneath the pleura and occasionally in the connective tissue around larger bronchi (secondary lymphatic tubercle).

(2) The coalescent nodules : these measure from 1-8th to a 1-4th inch in diameter, and are simply made up of groups of the smaller broncho-pneumonic foci welded together by a small amount of richly-nucleated fibrous tissue. The largest, situated at the apex, are about the size of a split pea ; they are solid caseous masses partially encapsuled by fibrous tissue. The pulmonary tissue between all these various scattered foci is quite crepitant

and in a fairly normal condition in this early stage, and the pleura not thickened, except at the extreme apex over the caseous nodules.

Now, in no part of the affected lung could I find those patches of pneumonic infiltration as large as a walnut in size, and presenting on section the uniform greyish-red, granular aspect, such as were described in caseous pneumonic phthisis. Neither was the stage of cavity formation reached in these cases. In two there was very early apical infiltration in the other lung, whilst in the third the extent of the disease was nearly the same in both.

So far then, in this early stage it is not a difficult matter to follow out the origin and evolution of the morbid process. Most pathological histologists are agreed in fixing the place of its commencement in a bronchiole or in its infundibular expansion into the alveoli connected with it. Here the tubercle bacilli settle, and as a result of their irritating influence proliferative changes are set up successively at different points in the wall of the bronchiole. While fresh ones are developing the older ones are caseating, and thus the lumen of the bronchiole or its infundibulum becomes blocked by a caseous mass. By the peripheral extension of the proliferative process to a number of the alveoli around, a nodule of broncho-pneumonia is formed. But the caseous degenerative changes follow in the same order. The wall of the bronchiole and the alveoli immediately contiguous become so affected by it that only the bare outlines of the framework remain. Around this caseous part is a more or less broad zone where the marked thickening of the alveolar walls by a kind of adenoid growth has become so blended with the cellular exudation within them that it is only in good preparations one can differentiate the *inter* from the *intra* alveolar changes that seem to go hand in hand with each other. And it is in the indeterminate character of this

zone that one may discern a tendency to the limitation of the process, but it is at the most an imperfect one.

The Modes of Extension of the Disease.

You will observe that the primary distribution of the disease in the scattered nodules of broncho-pneumonia around the terminal branchings of the bronchi is essentially a peripheral one. Its further extension in the lung from each of these foci takes place *by continuity of tissue* in two ways: (1) inwards or backwards from the bronchioles towards the larger branches distributed to individual lobules (intra-lobular bronchi), and then again from these by a repetition of the aspiration of the virus peripherally to *other* bronchioles or infundibular terminations within the same lobule. In this way by an alternate centrifugal and centripetal distribution an entire lobule may become involved:—(2) by the development of secondary interstitial tubercles following the course of the lymphatics in the perivascular and perilobular connective tissue, but especially in the adventitia of the small arteries and veins accompanying the bronchial ramifications, so that we find some of these blood vessels thickened and obliterated. These perivascular and perilymphangitic lesions are the true miliary interstitial tubercles, and are usually found associated with chronic tubercular phthisis. Their development is slow and gradual, but to their effects in obliterating the vessels must be attributed in some measure the necrosis and disintegration of the interstitial tissue in the midst of which necrotic or caseous masses are found.

Now in such a continual extension of the disease within limited areas of pulmonary tissue, it is obvious that these individual foci by their coalescence, may result eventually in the formation here and there of a considerable patch of tuberculisation around a

bronchus of a fairly large size. Its walls have already become thickened and weakened hy inflammatory cell infiltration, so that it is dilated, and eventually some part of it hecomes involved in the tissue disintegration going on in and around it, until it comes into direct communication with the softened caseous focus. In other words, a cavity is formed containing infective material which mingles with the catarrhal secretion in the hrcnchus and is, in part, expectorated with the mucopurulent sputum. In this elimination of the caseous material lies another danger, viz., that of a wider infection of distant parts of the lung (auto-infection). The infective sputum is not entirely got rid of; part of it may be arrested in another comparatively large branch of the bronchial tree near its root, whence it is liahle to become again aspirated into, and distrihuted to some other distant part of the lung which up to this time was free from the disease. In a similar manner the other lung may become affected by sputum reaching its hronchi and being aspirated into it. Such is the picture I have attempted to draw in order to explain the anatomical progress of a case of *chronic tubercular broncho-pneumonia.*

The pleura hecomes implicated early by extension from affected lohules situated immediately beneath it, and also through the anastomosis of its lymphatic apparatus with the lymphatics in the interlohular septa; in this way a chronic pleurisy is set up resulting in the thickening and adhesion of the pleura, which is constantly associated with chronic phthisis. In some cases you will find even evidences of a recent pleurisy (fihrinous exudation), distributed in patches, and engrafted upon the chronic. Such patches will explain the pleuritic friction sounds frequently heard in phthisis. If we hear in mind the reactive inflammatory changes implicating chiefly the interstitial tissue, which, in some degree always accom-

pany the tubercular process, we can now interpret and follow the varied anatomical changes seen on the post-mortem table in the lungs in these advanced and chronic cases.

We find one lung affected almost throughout its extent. Its pleura is thickened and adherent, it is more or less riddled with cavities, large or small, some of which are simply dilated bronchi, others the result of the softening and breaking down of coalescent patches of tubercular infiltration. There is a general thickening of the fibrous framework of the lung, so that the lung appears intersected in various directions with bands of newly formed connective tissue, given off from the thickened pleura, and anastomosing with the peri-bronchial and perivascular fibrous tissue. One feature about this tissue is, that it is never firm and white, or cartilaginous in consistence like that seen in cases of chronic fibroid phthisis of long duration. It looks swollen, vascular, and succulent, pinkish grey in colour, and on microscopic examination the cell elements predominate largely over the fibrous. It is more an inflammatory cell infiltration of the tissue in which the process of organisation is in quite an early stage. Hence the lung is seldom much contracted in bulk. Should part of it be free, and should there be a considerable amount of serous fluid in the pleural cavity, this free portion may be collapsed from pressure of the fluid. I have several times seen this condition. As to the other lung, its upper lobe or a great part of it may be quite as extensively affected. But wherever any crepitant lung is left, it is never entirely free from disease, usually it is the seat of discrete or conglomerate grey tubercles, the tendency of which, however, is not to caseate but to undergo a fibroid transformation (interstitial tubercle or tubercular perilymphangitis).

Occasionally this variety of phthisis, after its usual

insidious onset, takes on unexpectedly an acute course, and death ensues within six or eight weeks after the change in the clinical aspect of the case has set in, with a more or less sudden aggravation of the symptoms and physical signs. On referring to my notes of a few cases of this kind illustrating the sudden change in the type of the disease, I find that two of the patients had gone through acute attacks of pulmonary inflammation (bronchitis and pneumonia) twelve or eighteen months before the symptoms of phthisis became manifest. Although both patients asserted that they made a good recovery and enjoyed an interval of comparatively good health before the phthisis developed, it is quite possible that the acute attacks of bronchitis in the one, and of pneumonia with acute pleurisy in the other case, laid in some measure the foundation for the development of the phthisis, for neither gave the slightest evidence of hereditary taint. These patients attributed the exacerbation of their symptoms to "a fresh cold on the chest.' In other patients there was a definite family history of tubercular disease.

On post-mortem examination the fatal element appeared to be the development of an acute pneumonia which lighted up the tuberculosis into fresh activity ; for in two of the cases I detected tubercles in the liver, spleen, and kidneys, and to some extent, in the peritoneum ; certainly they were very sparse in the viscera, and not readily seen.

Although no cerebral symptoms were noted I examined the brain carefully in all the cases for tubercles, but with negative results. As regards the morbid anatomy of the pulmonary lesions, the lungs on section in the two cases above mentioned presented more or less extensive tracts of a recent red and greyish red hepatisation, midst which discrete and racemose groups of soft grey tubercle were imbedded. In the upper lobe of the most affected lung the tubercles and the pneumonic infiltration around

them were softening and breaking down to form small cavities. This lobe was bound down to the thoracic wall for the greater part of its extent, but the remainder of the lung was free and the pleura extensively affected with acute fibrinous inflammation, the layer of exudation on it being quite thick in places like that in acute pleuro-pneumonia. But on scraping it away, the pleura was distinctly beset here and there with miliary tubercles. The interest of these cases is their position on the border-land of acute general tuberculosis. I should mention that tubercle bacilli were very numerous, especially in the pneumonic parts immediately around the tubercles.

III.—The last variety of phthisis. with which I shall conclude my description, is the most chronic form of all, viz., Fibroid Phthisis..

Cases in which it is found may be conveniently classed into two groups :—

I.—Those where the fibroid changes have succeeded to the tubercular. At the close of the last lecture I cited a case of this kind, where the transition was marked. But we may also meet with cases where the fibroid changes are still further advanced. Large multilocular or sacculated cavities are then found at both apices, and the entire lung on one side may be considerably contracted by fibroid induration. Dilated bronchi with dense fibroid walls are also seen, and in the indurated tissue between them a few caseous or cretaceous deposits are found as the only vestiges of the tubercular affection. In the other lung that may be less affected, a certain amount of aerated pulmonary tissue is left, but even this is affected with patches of nodular induration, which consist microscopically of closely aggregated nodules of broncho-pneumonia that have undergone marked fibroid induration. Thus the small caseous centre in each corresponds with the lumen of a bronchiole, and is surrounded by a broad zone of dense fibro-nucleated and

pigmented connective tissue, through the medium of which the individual nodules become contiguous with one another. In other parts they are disposed in more isolated and smaller groups.

It would seem that most of the caseous material had been eliminated in these cases. Nevertheless the presence of these large cavities is strong presumptive evidence of the tubercular character of the primary mischief.

In another class of cases belonging to this group the tuberculosis is obsolete and so come upon accidentally. If the infiltrated patch is situated near the surface, the pleura over it is usually depressed by a stellar cicatrix. On making a section through it, one finds small caseous foci circumscribed by indurated and pigmented fibroid tissue. We may even discover a small cavity with dense fibroid walls and scattered immediately around it little caseous masses or fibroid tubercles.

In the case of a man who died of uræmia from granular kidney, I found an old encapsuled caseous and cretaceous node about the size of a walnut at the apex of the left lung; and spreading from and around it were a number of slatey-grey miliary tubercles, isolated or in small groups. Microscopically some were nodules of caseo-fibroid bronchitis or peribronchitis, others pretty specimens of the giant-celled tubercle. I do not remember to have seen a more exquisite example of a secondary localised miliary tuberculosis around an old caseous focus than that presented in the above case. In two others the tubercular disease was definitely limited to the pleura, which was thickened and studded all over with miliary granulations (anatomically giant-celled tubercle). Such instances as these of latent and obsolescent tubercular disease of the lung occur much more frequently than is generally believed.

II.—In the next class of cases the pulmonary affection is primarily non-tubercular. It is, in fact, a chronic interstitial pneumonia, described in the text-books as cirrhosis or fibroid induration of the lung ; and it arises out of a number of morbid conditions affecting the lung of which the following may be enumerated as the chief :—

a. From a chronic pleurisy as a pleurogenic interstitial pneumonia.

b. As the termination of an unresolved lobar and lobular pneumonia.

c. From chronic bronchial catarrh (winter cough).

d. As the result of the inhalation of dust particles of various kind, setting up chronic peribronchitis and lymphangitis. The diseases belonging to this group are classed together under the term pneumono-konioses—and includes miners', stone masons', and grinders' phthisis.

e. Lastly, the late Dr. Corrigan, of Dublin, described a primary or idiopathic form of interstitial pneumonia, with which I am not as yet practically acquainted.

Now, it is quite possible for any of the cases enumerated in the above groups to become tubercular at some period during the progress of the disease by infection with the tubercular virus. In fact, it is this liability which constitutes the danger in these cases, for the establishment of tubercular disease is often quickly followed by a fatal termination. As you are aware, diabetics are not infrequently affected by a caseous pneumonic phthisis, which Dreschfield and others believe to be non-bacillary. That it may be so at its commencement is quite possible, but in every case I have examined so far, I have succeeded in finding tubercle bacilli.

This concludes the description of the morbid anatomy of the lungs in the various forms of pulmonary tuberculosis.

I have now a few facts to relate in connection with

the concomitant lesions affecting other viscera, for without some reference to them, I should feel that these lectures on the pathology of phthisis were incomplete.

Condition of the Heart in Phthisis.

Size.—In 77 per cent. of the total cases the heart was described in the post-mortem records as "smaller than normal," and it was only in chronic fibroid phthisis with bronchiectasis that an enlargement was noted with some degree of hypertrophy and dilatation of the right side.

A small heart is usually mentioned in text books as one of the predisposing causes of phthisis, and it is a noteworthy fact, that notwithstanding the morbid changes in the lungs it remains small in the majority of cases. So far as my acquaintance with the literature of the subject goes, I do not remember to have come across any discussion or explanation of this fact. I need hardly remind you that, next to pronounced mitral stenosis, the most fruitful causes of right-sided hypertrophy and dilatation are emphysema, chronic bronchitis with bronchiectasis, and fibroid changes in the lung, and hence it is interesting to note that a certain degree of dilatation was associated with some of the cases of fibroid phthisis.

It is, however, in the acute, sub-acute, and the less chronic varieties of phthisis, that the heart remains small or even undergoes atrophy to some extent. Possibly it is to be referred partly to the quiescent mode of life which patients suffering from phthisis are compelled to lead from the time the symptoms become troublesome, so that no extra stress is thrown on the heart. Then again the amount of blood must be relatively diminished, as indicated by the general anæmic condition of the patient and the emaciation that is taking place. Thus the heart gradually accommodates itself to the needs of the organism generally, and the

right side to the alterations of the pulmonary circulation in particular. In a case of chronic bronchitis and emphysema or of fibroid phthisis, the patient may be able to go on with his employment for some time before compensation fails, and œdema begins to show itself; while in tubercular phthisis the patient soon becomes totally unfit to follow his employment on account of his febrile condition and general malaise; it is not usual to see signs of œdema in phthisis except perhaps in the last stages when the kidneys are usually affected.

Cavities and Valves.—The right side was generally engorged with blood clot, most commonly with post-mortem or "agony" clot; but in a few cases ante-mortem thrombus was found extending into the pulmonary artery.

Valves.—In two cases there was thickening of the mitral with stenosis of the orifice (rheumatic in one, and probably congenital in the other case). In two other cases, recent acute verrucose endocarditis of the aortic and mitral valves.

Pericarditis.—Tubercular and acute in two cases with sero-purulent exudation in the sac; chronic with pericardial adhesions in three cases. In two of these the heart was displaced by the adhesion of the pericardium with the thickened pleura of a contracted left lung.

Cardiac Muscle.—Described as looking fairly norma in 50 per cent.; brown atrophy specially noted in 30 per cent. In the remaining 20 per cent., it was noted as soft, pale and friable with a distinct yellowish mottling, and a microscopic examination of the fresh muscle, which was made in several of these cases, showed marked granular and fatty changes in groups of muscle fibres (patchy degeneration).

Condition of the Kidneys.—Anatomical changes, though for the most part slight, are frequent in the kidneys in phthisis.

Excluding cases of tubercular pyelonephritis, of lardaceous disease, and those advanced cases of granular contracted kidney, which constituted independent affections, the following analysis of the remaining cases is of some interest.

(A) Kidneys swollen, but capsules strip well, cortex increased, pale, semitranslucent with greyish yellow mottling, = chronic parenchymatous nephritis: six slight cases and two marked, where the kidneys were early large white. Microscope showed the changes to be chiefly intra-tubular, viz., cloudy swelling and granulo-fatty degeneration of the epithelium of convoluted tubules.

(B) Kidneys enlarged, capsules partially adherent (here and there), cortex swollen of a pale yellowish grey but mottled, with hyperæmia, = sub-acute or chronic diffuse nephritis (interstitial and parenchymatous changes): Eight slight cases, two marked in which sub-acute glomerulitis was a conspicuous change.

(C) Kidneys smaller than normal, capsules, a little thickened and more or less universally, though slightly adherent, surfaces finely granular, cortex narrowed in places, and uneven in outline = slight interstitial nephritis: seven cases. Microscopical examination of some of the kidneys taken from groups B and C showed well-marked interstitial changes, *i.e.*, small-celled infiltration of the stroma around glomeruli, and around the arteries and veins in the labyrinth. These changes were quite patchy in distribution throughout the cortex; but there was *no very pronounced thickening* of the small arteries, such as is characteristic of the arterio-sclerotic or red granular kidney. Here and there changes were found affecting the glomeruli, such as intra-capsular cell proliferation and exudation, and slight pericapsular thickening, a few were undergoing hyaline fibroid change.

These were evidently slight cases of interstitial nephritis secondary to the pulmonary affection.

Miliary tubercles were found associated with the nephritis in some cases.

Liver.—The most constant and prominent change in all cases was "fatty infiltration," fatty liver. *Where the tuberculosis was localised in the lungs*, I rarely met with amyloid infiltration, although I carefully looked for it in every case where I suspected it might be present. On microscopic examination scattered miliary tubercles are more frequent than one might suppose, for unless they are present in the serous capsule they escape detection by the naked eye. Perihepatitis was found in the cases where the peritoneum was the seat of tubercular infiltration, and also in those where it was localised to the pleura, whence it had apparently spread to the peritoneal covering of the liver through the diaphragm. Exceptionally the liver was found to be slightly granular and cirrhotic. In one instance a latent tubercular disease of the lung was found associated with a typical case of cirrhosis of the liver with ascites.

Stomach.—Dyspeptic troubles are often prominent symptoms associated with phthisis. I have not myself made any histological examination of the stomach of phthisical patients, but one of the most recent contributions to this important subject is from the pen of Dr. Schwalbe, who made a careful examination of the stomach in twenty-five cases of phthisis, and found important changes in the mucous membrane in twenty out of the total number, viz., interstitial gastritis in fifteen, parenchymatous degeneration with dilatation of the tubules in four, and amyloid changes in one case. (47)

Intestine.—Tubercular disease in the form either of distinct ulceration or infiltration with miliary tubercles was noted in 54 per cent. of the cases; of the remainder

reference to the intestine was omitted in a few, and disease noted as absent in the others.

Another note of interest is the relative frequency of the right and left lung as the one in which the disease was most advanced, and therefore the one in which the disease first appeared. Left lung in 51 per cent., right in 49 per cent. of the cases, or practically equal.

Lardaceous disease was found more or less generalised, mainly in those cases where the pulmonary affection was associated with tubercular disease in other parts of the body, but especially with bone disease, in 25 per cent. of the cases.

Complications.—Pleurisy frequent, but pneumothorax and pyo-pneumothorax in only four cases out of the total number.

Death directly from hæmoptysis in the later stages of the disease occurred in three cases only.

Concluding Remarks.—If we review our subject in the light of the great advances that have been made in the pathology not of tuberculosis only, but also in the pathology of infective micro-parasitic diseases generally, much less importance must be ascribed to the characters of the anatomical changes as distinguishing features of the disease, than to the presence of the bacillus, *which is the only reliable test of what is tubercle.* Even if we accept the older views of pathological anatomists, that the demonstration of a definite structure is the *sine quâ non* for the proof of tubercle, and if this structure is the *so-called reticular giant-celled* tubercle of Schüppel and others, then I must admit that my experience leads me to point out its relatively rare occurrence in the lung compared with the generalised inflammatory lesions of a totally different structure. Secondly, when it does occur it is far more frequently as a secondary, than as a primary, event. We have seen that as a primary lesion it occurs in some

cases of acute miliary tuberculosis, but that it is nearly always secondary in chronic tubercular phthisis, and is mingled with other inflammatory formations. Then, again, the exclusiveness of this anatomical distinction of tubercle is broken down by the fact that almost identical structural formations are found in other diseases, in syphilis, in ordinary granulation tissue, and as the result of the presence of other parasites, such as actinomycosis, and strongylus in the dog. Even if we regard as anatomically true tubercles those minute foci of cell accumulation which develop in the walls of the bronchioles as the initial step in tubercular bronchitis and broncho-pneumonia, we seldom if ever meet with them in the perfection of their development as giant-celled systems. I have often seen them in the sub-epithelial tissue bulging into the lumen of the bronchus simply as a mass of cells, but never yet seen that remarkable differentiation of structure so beautifully depicted in the illustrations in pathological text-books. I may say that out of many hundred slides I have only a few where this remarkable differentiation is typically shown in the so-called true miliary tubercles, and I keep them as treasures and relics of the teaching of days gone by.

In the bronchial wall they degenerate as quickly as they grow, and at once excite an inflammation around them—an inflammation distinctly pneumonic in type, which I regard as *inseparable* from the process as a whole. We have had abundant proof of the varied, and at the same time exceedingly interesting characters of the lesions making up the sum total of pulmonary phthisis, and have seen that *in the main* they are essentially inflammatory in character, and either specific or simple. *The specific are caused directly by the bacilli*, and according to their anatomical form, we may designate them bronchitic or peribronchitic, pneumonic, either broncho or lobular, or interstitial, but at the same time we should

qualify them by the adjective "*tubercular*," when tubercle bacilli are present in them. So long as they are tubercular, I really cannot see what objection there is in calling them "*large soft grey*" and "*yellow tubercle*" (as Dr. Green still does in the latest edition of his text-book), leaving the term "*firm grey miliary tubercle*" (48) to distinguish the reticular giant-celled formation. The simple inflammatory lesions are mainly represented by the reactive or reparative changes taking place in the connective tissue framework. The explanation why in some cases we get a rapidly spreading acute lobular pneumonia, and in others a chronic disseminated broncho-pneumonia is to be referred, as I have previously mentioned, to the amount and intensity of the virus propagated in the lung at a given time.

Lastly, as to the mode of origin of tubercular phthisis and the influence of hereditary predisposition, I believe that in the majority of cases it is primary by way of the respiratory tract in individuals possessing a strong hereditary taint. And on this point I cannot agree either with Cornet, who would blot out "constitutional predisposition" from amongst the etiological factors, or with Baumgarten, who believes that it means an actual transference of the virus, and that nearly all cases of phthisis start from some latent focus indirectly through the lymphatic system.

With regard to the pathological chemistry of the disease, which is now an all-absorbing question, I have referred to the experiments of Maffucci with the sterilised chemical products of the growth of the bacillus in nutrient media; and I must not omit to refer to important experimental investigations with the chemical extract from phthisical sputum, conducted by Dr. Philip of Edinburgh, who is already a well-known clinical authority on pulmonary diseases, (49) as well worthy of your perusal.

NOTES.

(1) "Traité du diagnostigue des maladies des poumons,' 1819

(2) "Etudes sur la Tuberculose," 1868.

(3) *Practitioner*, Vol. xxix, contains an account of experimental investigations made in 1868-9, and a critical review of the previous researches of others, and full literary references.

(4) "On the Artificial Production of Tuberculosis in the Lower Animals." Loudon: Macmillan. 1868.

(5) "Die Tuberculose vom Standpunkt der Infections-lehre, also Lectures on Path. Trans., by McKee. Sydenham Society Series.

(6) See "Selected Essays on Bacteriology," edited by W. Cheyne, Syden. Soc. New Series. Translations of German Monographs, art. Tuberculosis, trans. by Stanley Boyd.

(7) "Centralblatt f. d. Med. Wiss, No. 15, 1881. Aufrecht had also about this time discovered similar bacilli (Path. Mitth., 1881). For newest information on the histology of tubercle and the relations of the bacilli, &c., see Baumgarten's recent work, "Lehrbuch der Pathologischen Mycologie" Vol. II. 1890.

(8) These hopes have been fully realised in the investigations conducted on bacteriological lines by Baumgarten, Schottelius, Tappeiner, Weichselbaum, and other experimenters since the discovery of the bacillus.

(9) "Green's Pathology and Morbid Anatomy."

(10) "Selected Works," Sydenham Society, Old Series.

(11) "Virchow's Onkologie," Vol. II. The grey granulations only of Bayle, or the small firm grey tubercles of recent writers were regarded as typical and true tubercle in this anatomical sense.

(12) A view no longer held though it was apparently supported by Beale, vide Discussion at Path. Soc. of London, "On the Anatomical Relations of Pulmonary Phthisis and Tubercle," Path. Trans. 1873.

(13) "Lungenentzündung Tuberculose und Schwindsucht, München, 1873.

(14) "Untersuchungen uber Lymphdrüsen-tubercle, Tübingen," 871.

(15) "General Pathology" (American Translation).

(16) "Virch. Arch." B. 42.

(17) "Studien über Tuberculose Berlin," 1873.

(18) "Untersuchungen über Lungenentzündung, &c. Hirschwald," Berlin, 1873. "Ueber locale Tuberculose, Volkmann's Sammlung," No. 64.

(19) "Recherches sur l'Anatomie Pathologique de la Tuberculose." Paris: Masson, 1873.

(20) L'Union Medicale, 1881.

(21) "Manuel of Path. Hist. Trans.," by Alice Hart.

22) "Lymphatic System of the Lungs," (Part II of the Anatomy of the Lymphatic System). London.

(23) "Path. of Bronchitis, Pneumonia, and Tubercle in the Human Lung." Macmillan, 1881. Reprint of papers in the *Practitioner*, 1879-81.

(24) *Practitioner*, 1883. An excellent summary of the views of Pathological anatomists up to 1868, by Prof. Waldenburg in his monograph, "Die Tuberculose." Berlin: 1869. And in an article in the *Berlin Klin. Wochenschrift*, 1874, No. 25.

(25) "Mugge. Virch. Arch," Vol. lxxvi. Arnold 1b, Vol. lxxxviii. Weigert 1b., Vol. lxxvii, and lxxxvii, and civ. *Cornil, Journal of Anatomy*, 1880. (26) *Loc. Cit.* (27) *Loc. Cit.*

(28) Ueber die Entstehung der Riesenzellen im Tuberkel." Wagner's *Arch. d. Heilkunde*, vol. xiii.

(29) "Lehrbuch der Allgemein und Speciellen Pathologie," 6th ed. 1880. Articles 118 and 119.

(30) Mikro-organismen bei den Wundinfections-Krankheiten des Menschan. Wiesbaden, 1884.

(31) It will be seen that the current of my thoughts are centered around the bacillary theory, which is still the burning question of the day in the etiology of the disease, and that I have not attempted to discuss some of the ordinary and well known factors in the etiology, such as age, sex, occupation, and climateric conditions, &c.

(32) Vide references in Lecture I.

(33) "On Pulmonary Phthisis," Textbook of Practical Med., American translation.

(34) References in first lecture. I should have mentioned that the supposed production of tubercle by the inoculation of animals with non-tuberculous material, and by the introduction of setons and other foreign bodies, tended to shake the conception of the specific nature of tubercle, and to favour the assumption that any form of irritant, caseous, purulent, or otherwise, was capable of originating tubercular disease. Various fallacies were subsequently proved underlying such experiments, and in the light of the tubercle bacillus, the lesions in many instances were shown not to be tubercles, but formations allied to those of chronic pyæmia. In other cases the possibility of contamination of the material introduced with tubercle bacilli, was demonstrated, and the lesions were examples of a mixed injection.

(35) The subjoined references will suffice to show the differences of opinion amongst well-known authorities with respect to the significance of tubercle bacilli in the sputum and lung and also concerning the etiological identity of miliary tuberculosis and phthisis:—In support of Koch's views. Baumgarten Zeitschrift f. Klin Med., Bd. ix, 1885 Lehrbuch der pathol. mycôlogie, 1890. Art.—Tuberculose, vol. ii. Ziegler Ueber tuberculose und Schwindsucht. Volkmann's Samml Klin vortrage, 151. Orth., Lehrbuch der speciellen Path. Anatom.,

1887. Poeten, Experiment untersuch über. Lungen schwindsucht und tuberculose. Dissert, Göttingen, 1883. Die verbreitung der tuberculose in den Lungen. Schaeffer, Dissert, Berlin, 1884. Wesner, Deutsch, Archiv f. Klin. med., xxxiv, 1884 and Muhlert, Dissert, Göttingen, 1885; Ueber das Vorkommen von Bacillen in miliartuberculosen und phthisischen Veränderungen. Germain Sée de la phthisie bacillaire des Ponmons, Eng., trans. by W. H. Weddall. Kegan, Paul, Trench and Co., London, 1886. Watson, Cheyne, loc. cit. Pulmonary Phthisis, by Dr. James, Edin., 1888. Ueber Tuberculose, &c., &c., by Dr. George Cornet, Leipzig, 1890. II. Against Koch's views:—Arguments against the identity of miliary tuberculosis and pulmonory phthisis and in support of the view that phthisical changes are not casually dependent on bacilli. Anfrecht. Pathol. Mittheil, vol. ii., 1883. Virchow's later views, Arch. Bd., 1889, and Berlin. Klin. Wocheuschrift, 1883. Langerhans, Arch. Bd., 97, 1884. Gibbes and Shurly. An investigation into the Etiology of Phthisis. Part I. Reprint of Papers in the American Journal of Medical Scieuces, March to August, 1890.

(36) Baumgarten refers to the experiments of Maffucci, who inoculated the eggs of fowls with the microbes of chicken cholera, anthrax, and the pneumo-coccus of Friedländer, and then artificially hatched them. The fate of the micro-organisms, so long as the embryoes lived, was variable. Some perished owing to the resistant vital energy of the growing embryonic tissue, and in no case was there observed a growth of the microbes either in the embryonic tissue itself or in the surrounding nutritive fluid, on the other hand some of the organisims appeared to remain in a latent virulent state, until the terminatiou of the embryonal development, to manifest their activity during post-embryonic life, and to call forth outbreaks of the disease. Bearing, too, on the question of hereditary transmission are the observations of Johne, who demonstrated tubercle bacilli iu the fœtuses of calves; of Jani and Wiegert, who found them in the vesicular seminales and in the seminal tubes of the testes of tubercular men, when these structures appeared to the naked eye otherwise healthy. Jani found them also in the vagina and in the Fallopian tubes of phthisical women. This is a field of inquiry still open for further investigation. Johne, Fortschritte der Medicine, 1885, No. 7 Weigert and Jani, Virch, Archives, Bd. 103, 1886.

(37) Baumgarten says that a primary tuberculosis of the gastro-iutestinal tract rarely occurs in man. This is not to be explained by supposing that the intestine could act as the portal for the entrance of the tubercular virus without becoming affected itself, and that the bacilli, having passed unopposed through the intestinal wall and the mesenteric glands, succeed in reaching more distant organs, where they set up changes. Such a supposition is contrary to experimental evidence, which shows that in intestinal tuberculosis the mesenteric glands are always, and it may be, extensively affected. Although primary intestinal tuberculosis is comparatively rare, tubercular

disease of the mesenteric glands is of frequent occurrence in children. Vide the interesting lecture on Tuberculosis and Tabes Mesenterica, by Dr. Sims Woodhead, *Lancet*, 1888, Vol. II, pp. 51 and 99, where statistics are given. Baumgarten says the rarity of a primary tuberculosis of the gastro-intestinal tract is to be explained by the insignificance of the exciting causes.

(38) The works of Wilks and Moxon, Gall and Sutton, and others.

(39) "The Principles and Practice of Medicine," by C. H. Fagge.

(40) Vide Postscript.

(41) Ueber die Wirkung der reinen, sterilen culturen des Tuberkel bacillus. Centralblt. fur Allgemeine Path. u. pathologische Anat., 1890. Bd. 1, No. 26.

P.S.—In preparing these lectures for the press, I have come across the report of an exceedingly interesting and unique case recorded in Ziegler's Beiträge zur. path., anat., und., allg., Pathol., 1891, p. 429, by Birch-Hirschfeld and Schmorl, of the direct transmission of the bacillus tuberculosis from the mother to the fœtus. This is claimed to be the first case of the kind recorded in the human race. Klebs in the last edition of his text book on "Allgemeine Pathologie," has put forward the view of the possible infection of the fœtus in utero by its swallowing liquor amni contaminated with tubercle bacilli.

(42) In three cases of spinal caries there was a direct extension of the disease to the lung.

(43) I have emphasised this, because, in regard to this point, every pathologist of experience knows, as the result of his observations, that the extent of the disease as mapped out during life by physical diagnosis frequently does not correspond with the actual extent of the disease found in the post-mortem room, in other words, it often falls far short of it, and thus the terms "clinical signs of very early or of a fairly pronounced phthisis" convey to the pathologist only a proximate estimation of what the real anatomical extent of the disease may be.

(44) Without wishing to disturb the gastronomic feelings of my readers, I may compare such a lung on section to a cake of a reddish brown colour which is everywhere stuffed with pieces of almonds representing the opaque yellow patches.

(45) I have not been able to make out in these caseous parts the thickening of the alveolar walls by an adenoid growth in them, upon which the late Wilson Fox laid such stress as representing the true tubercular lesion. The walls degenerate contemporaneously with the exudation included within them.

(46) "Diseases of the Lungs," 3rd Edition.

(47) "Die Gastritis der Phthisiker vom pathologisch-anatomischen standpunkte." Virch. Archiv. Bd. 117; Heft 2. See also yearly Retrospect, *British Medical Journal*, December 28th, 1889, pp. 1,417.

(48) "No doubt the term 'tubercle' is an unfortunate one; but it has been handed down from one authority to another, and we have

become so accustomed to it, that it would be difficult to replace it by any other word. Moreover, since Koch's discovery its signification is not limited to structural detail, but includes now a distinct reference to the organism causing the disease."

(49) "Pulmonary Tuberculosis," by R. W. Philip, M.A., M.D., F.R.S.E. Edinburgh and London: Young J. Pentland. 1891.

ERRATA:—

Page 53, line 4 from bottom, "tubercle bacilli was found" should read "tubercle bacilli *were* found," &c.

Page 56, line 19, "*hæmoptæ*" should read "hæmopt*oe*."

Page 58, line 12, "marked" should read "masked."

Page 65, line 9 from bottom, "In this caseous tracts where interstitial changes are absent, *the* explanation," should read "In *these* caseous tracts. . . . . *this* explanation," &c.

Page 67, line 8, put comma after extensive.

Page 68, line 17, "*bronchietic*" should be "*bronchiectatic.*"

T. W. Danks & Co., Steam Printers, 71 Dean Street, Soho Square.